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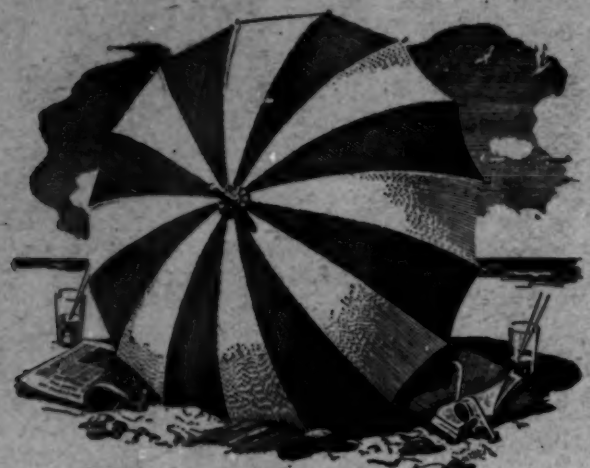

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BRITISH MEDICAL JOURNAL

LONDON SATURDAY JULY 10 1954

British Medical Association

ONE HUNDRED AND TWENTY-SECOND ANNUAL MEETING, GLASGOW, 1954

President's Address

THE PRACTICE OF MEDICINE

BY

Sir JOHN McNEE, D.S.O., M.D., D.Sc., LL.D., F.R.C.P., F.R.F.P.S.

Emeritus Regius Professor of Practice of Medicine, University of Glasgow

Until last year I had occupied for 17 years the Regius Chair of Practice of Medicine in the University of Glasgow. This is an unusual definition of a Chair, only duplicated, so far as I am aware, at Trinity College, Dublin. I do not know when or why this special description was adopted in Glasgow—it was not always so. On my appointment, however, I took the words to mean exactly what they say and that my main duty, but certainly not my only duty in the University, was to train students for medical practice.

Medical practice is a broad term, but by far the majority of our profession are actively engaged, directly or indirectly, in some form of practical work involving the health of individual patients or of the community. The largest group are family doctors, but many work in hospitals, in various branches of the public health service, and in the numerous specialties chiefly but by no means entirely concerned with diagnosis—radiology, pathology, bacteriology, biochemistry, and others. In what our President of 1948, Sir Lionel Whitby, described as "The Changing Face of Medicine," all of us have new problems to face, and particularly the blending of the old with the new in the practice of medicine. It is about such matters that I wish briefly to speak.

Previous Meetings in Glasgow

The British Medical Association, founded in 1832, has twice previously held its Annual Meeting in Glasgow during its 122 years of service. The more recent meeting, in 1922, was presided over by one of my own most distinguished teachers, Sir William Macewen, whose address on brain surgery was a wonderful exposition of a branch of surgery in which he was a pioneer. The first meeting, in 1888, was under the presidency of a great scholar and physician, Sir William Tennant Gairdner, my predecessor from 1862 to 1900, and twelfth-in-line in the ancient Chair first founded in Glasgow University in 1637. I naturally did not know Gairdner, but I have known many of his pupils, and some of them were my teachers. All were agreed about his wide classical learning, his great clinical knowledge and experience, and also (in his later years at least) about his astonishing absent-mindedness.

Gairdner chose as the subject of his presidential address "On the Physician as Naturalist," and the deep meaning of these words impressed me long ago as they have impressed others. Almost the same words were used, with due acknowledgment, and different aspects of the same idea were developed, by John Ryle, of Guy's Hospital, Cambridge, and Oxford, in his book *The Natural History of Disease*, first published in 1936. Recently, Sir Macfarlane Burnet, one of our great modern exponents of the viruses, has published a new edition of his book on the *Natural History of Infectious Disease*, and there are many other examples illustrating the merits of Gairdner's theme.

Why did Gairdner choose this title for his address? His choice clearly derived from two sources—the scope and character of his professional work as a physician *of his time*, and his love and knowledge of the classics. Let me remind particularly the lay part of my audience that when Gairdner addressed the B.M.A. in Glasgow in 1888 the cause of most of the acute infective diseases was quite unknown. Gairdner, therefore, with his contemporaries, watched the natural course of an illness, and, being a trained naturalist, he noted the differences between this and that illness. From previous observations on many patients he could thus arrive at the correct diagnosis; but in his day, as we all know, effective treatment was sadly limited. His early training in Edinburgh no doubt influenced him greatly, for there he had been deeply involved in the clinical differentiation of typhoid (enteric) from typhus fever—one, as we now know, due to a bacillus and the other to a rickettsial virus. In the absence of all knowledge of the essential cause, Gairdner could only watch the natural history of the outbreaks in the crowded and insanitary tenements, and observe that in their spread to other sufferers each disease bred true.

Gairdner also in his address laid stress on the classical derivation of the word "physician," and acclaimed him as essentially a student of Nature, in fact a natural philosopher, although the use of this term has changed and limited itself with time. In Glasgow, at least, our Professor of Natural Philosophy is now a physicist much concerned with the problems of atoms and atomic energy.

The Physician as Naturalist

Is it necessary still for the physician—and for my purpose to-day I can obviously include all the many branches and specialties in our profession among the physicians—to study the natural history of disease so closely? I wish to emphasize that for many reasons, only a few of which I can touch

on, it is as essential as ever, and remains the basis of all good medical practice.

It is true nowadays that in the practice of medicine must be added, but never substituted, all the new scientific discoveries about causation, methods of accurate diagnosis, and especially of treatment with which we have been blessed in the last fifty years. I shall return to these additions presently.

But first things still come first, and nothing should precede the careful clinical history of the patient from all aspects, then of his present illness, and finally the close search for symptoms and signs of disease. My long experience as a teacher of medical students, especially in the out-patient department of a hospital, has shown to me over and over again how frequently we can arrive at a complete and accurate diagnosis, which must necessarily precede treatment, by using the simple observational methods of the trained naturalist. I do not exclude here the simple instruments which every doctor carries, such as a measuring tape, a stethoscope, and a blood-pressure apparatus, for these only add precision to the clinical observations.

In many cases, however, further investigations are imperative both for complete and accurate diagnosis and for correct treatment. These essential additions must be made fully available to our patients, and constitute the great and fundamental difference between Medicine in Gairdner's day and in our own.

Thus both the old study of the natural history of disease and the new scientific discoveries and methods of the past fifty years must be carefully blended for the benefit of our patients, but *in their correct order.*

I mention here, to illustrate this point, the awful but no doubt apocryphal story of the interns who, when dealing with a very sick man, said, "Let us put him on sulphonamides for three days, and if he isn't well by then we had better examine him."

I would add that opportunities for the discovery of new diseases and new syndromes by the simple observational methods of the naturalist are not yet over, although of course they are more limited. I quote, simply as examples, my own experience with trench fever in the first world war, Q-fever, German measles during early pregnancy and its effects on the offspring, Bornholm disease; and there are others. I would remind you that it is to general practitioners and to men in different branches of the public health service that favourable chances of this kind are often first available.

I am well aware, in reference to what I have been saying, that the practitioner's reiterated complaint is of lack of time to examine his patients thoroughly, and in much of general practice as it exists to-day this is only too true. I personally cannot take a full clinical history and examine a patient in under half an hour at the very least, and in the final examination at the end of his training we always allow the student a full hour for his "long case." When the young graduate enters practice he will shorten this as his experience and skill increase, but the few minutes' time which may only be possible for the first examination in a crowded surgery to-day in Britain portends bad practice of medicine. It leads to slipshod work and slipshod thinking, and to the family doctor's responsibility being shelved in favour of expensive hospital investigation. This fault is no longer confined to general practice, for, as is inevitable, it has been infecting consultants with their increasingly busy hospital departments and clinics. This state of affairs cannot be allowed to go on, for it undermines the whole foundations of sound practice of medicine. The remedy is not easy, but many of you must, like myself, have been thinking hard about how to deal with it.

The Practice of Medicine and Modern Discoveries

The advances in medicine of the past fifty years have chiefly been derived from increasing knowledge in what are often called the basic sciences of medicine—anatomy and physiology, pathology and bacteriology, chemistry and biochemistry, physics, pharmacology, psychology, and others. This period naturally coincides with the great expansion of laboratories for teaching and research in our universities and medical schools; and I would like to add here, for it interests me so greatly, of laboratories and institutes of clinical investigation, mostly under the charge of university professors, but attached closely to the hospitals and to patients. It coincides also with the rise of the great research institutes for medicine, and those administered by the Medical Research Council may simply be quoted as an example.

It would be ungracious not to refer at this point to the abundant and fruitful research work undertaken in the laboratories of the great manufacturing and trading houses, which has provided us with so many new and valuable drugs. It is to them, indeed, that we finally owe our indispensable supplies of insulin, of antisera, of penicillin, and the control of their effectiveness and sterility.

The great scientific advances in modern medicine have recently been very fully described by two distinguished members of our profession, Lord Horder and Sir Henry Dale, and I myself have witnessed quite a large part of this golden age of progress. Many, but by no means all, of the triumphs of bacteriology had preceded me, but I must point out that one of its earliest triumphs, and certainly its greatest practical triumph, resulted from the work of Lord Lister, then Professor Lister, at the Royal Infirmary, Glasgow, from 1860 to 1869, which led to the safety of modern surgery. *X* rays were also discovered well before my time, but their progress as a handmaid of medicine has been revolutionary. I can easily remember the discovery of vitamins, and how we quickly learned to prevent rickets, of notorious frequency among the children in this city of Glasgow. These are just a few examples taken from a great era, and I can do no more than mention the many new laboratory methods which have advanced both our real knowledge of disease and our accuracy in diagnosis.

Our patients, however, apart from their knowledge of the safety of surgery, would naturally claim, sometimes from their own experience, that the greatest progress of all has been in the curative treatment of acute disease. The slow and gradual development of the work leading up to the appearance of our recent remedies is often forgotten, but we have recently been reminded of our facts by the centenary celebrations of the birth of Paul Ehrlich, the father of the whole conception of chemotherapy in disease. Salvarsan came into practical use about 1909, just as I was entering the medical profession. Then came a period of great therapeutic discovery, not to be classed as chemotherapy, including, for example, insulin, liver in pernicious anaemia, blood transfusion, followed by a return to pure chemotherapy with the sulphonamide drugs, penicillin, and the more recent antibiotics.

Ehrlich, as I have said, was the founder of modern chemotherapy, but at the centenary of his birth we recalled that he and his great contemporary von Behring were equally interested in the problem of immunity to disease—natural and acquired. Practical results of this pioneer work came from many hands, with results such as the introduction of antitoxic sera for diphtheria and tetanus, and the subsequent development of preventive inoculation which has almost rid us of lockjaw in war and diphtheria in our country in peace.

The recent triumphs of chemotherapy and the activities of the chemists in producing more new and synthetic drugs must therefore not be allowed to blind us to the great therapeutic possibilities of immunity, the natural way by which the body of itself, and by its own activities, overcomes disease.

If we knew—and many are actively trying to find out—the secrets of the natural process of immunity, we might add much more to our therapeutic array. Some of the results of passive immunity—that is to say, of antisera prepared from animals—in actual diseases such as tetanus and diphtheria have already been mentioned, but I cannot help

praising here the campaign launched by our Ministry of Health only one decade ago, which has resulted in the great majority of our children being actively immune to the terrors of diphtheria. This is indeed a perfect example of the applications of immunity in preventive medicine.

There must presumably be a limit to the number of the new and successful synthetic drugs which the chemist can provide for us, and, as we all know, these remedies are not without their dangers and difficulties, both from sensitization of the patient and from drug resistance—in a sense an acquired immunity of the invading microbes themselves.

There seems, however, no limit to the way in which research may increase our knowledge of the natural process of immunity for our therapeutic use. It may be remembered that at the present time many have turned to immunity in trying to find some safe and efficient prophylactic "vaccine" against influenza and poliomyelitis, diseases which are untouched by any drug or antibiotic which we at present possess.

In the ordinary practice of medicine the doctor cannot invent new drugs, but when watching the response of the body to disease he can still actively look for clues which might be of the utmost value to those of his brethren whose work keeps them within the walls of their laboratories.

So far I have been discussing mainly our greatly increased control over acute and infective disease, and I have also referred, but far too briefly, to the wonderful effects of replacing or restoring secretions of the normal body which have failed or gone wrong—insulin in diabetes, thyroid extract in myxoedema, and vitamin B_{12} in pernicious anaemia are a few examples.

Those of us engaged in the practice of medicine, however, do not need to be told that there are still many diseases, especially chronic diseases, in which we have so far made much less progress towards prevention and cure. Cancer obviously comes first into this category, but the chronic rheumatic diseases, chronic diseases of the nervous system, and even the ubiquitous chronic gastric ulcer are examples. Whether prevention or cure of each or all of these, when it eventually comes, will be from the chemist's laboratory, or by restoring to normal some natural functional activity of the body which has become deranged or "diseased," or by some development in immunity, we simply cannot foresee.

The Physician as Teacher

It might at first sight be thought that not all physicians are teachers, but only professors of medicine and consultants or specialists working in hospitals where medical students are taught. This, of course, is quite untrue, for every general practitioner is essentially a teacher, instructing his patients during illness and also, I would hope, on how to keep well. The courtesy term "doctor" by which we are addressed by our patients indeed implies that we are teachers, for that is the original meaning of the word. The status of the physician as teacher in general practice has become difficult, for medicine is news, and it is sad to see advertisements in the daily newspapers usurping the family doctor's place. It is therefore sound policy that the B.M.A. has founded the successful publication *Family Doctor* so that practising doctors themselves can provide authentic and unbiased information about health.

Other branches of the medical profession do not receive adequate recognition as teachers. The public health service, competent, unobtrusive, and therefore sometimes forgotten, has important duties in teaching and protecting the public as a whole. Its successes in preserving the public health are almost taken for granted until we compare our good fortune with what happens in less-developed countries.

We now come to the hospitals, and the teaching which doctors so constantly undertake within them. The teaching hospitals are mainly concerned with the training of our future doctors (and also doctors returning for further experience), but it is often forgotten that doctors are responsible, in part at least, for the training of nurses, almoners, dietitians, physiotherapists, radiographers, and laboratory technicians of many kinds.

My own activities as a teacher have chiefly been concerned with medical students, and many others like myself are gravely concerned with the problems of medical education for practice. In Gairdner's day the undergraduate course was four years, in mine five years, and now it is six years, plus one year in an approved hospital, plus (for males) two years in the armed Forces. The limit has clearly been reached and even surpassed, for the period of preliminary training is now longer than for any other profession. The extended time is of course due to the great increase in medical knowledge, and the question arises of how much the average medical student intending to enter practice must know and learn in his undergraduate career. To know all would require a lifetime, and much thought is at present being given, not in our country only, to finding the right answer.

The Physician as Investigator

Medical research interests all of us, and I want to say something about it with particular reference to the possibilities of research for those actively engaged in the practice of medicine. The word "research" must not be regarded as a fetish—all it means is search and research for the explanation of natural phenomena and how to control or alter them.

In medicine, it is now true to say that many of the problems of fundamental research are so difficult that they can be undertaken only in universities or special research institutes where the complicated and expensive apparatus is available. In most hospitals facilities for less intricate research are available, particularly, of course, in those closely attached to medical schools and universities. Research in general practice is a much more difficult problem.

I leave out the universities and research institutes and come first to the hospitals. I have no doubt that every teacher of medical students should, if possible, have passed through the discipline of research, for it is he who will keep alive the flame in his students. The modern clinical teacher, moreover, must know thoroughly the language and techniques of the laboratories, not only because he is so dependent on them in his work, but still more to interpret to his students the relative and absolute value of the results for diagnosis and treatment.

For many years I was actively engaged in research work, and later in directing and encouraging younger men to do it. I made no epoch-making discoveries, but I am not disappointed; for that privilege is given to few—perhaps, sometimes, with a little luck to help them.

It is instructive, I think, to meditate on how some of the great discoveries in medicine are made—very few of them come in a flash of inspiration. Consider insulin, and the many years between the fundamental work of Minkowski and Claude Bernard and the final discovery by Banting and Best. The wall of research which culminated in insulin was built up stone by stone by many splendid workers, and could not be hurried until finally it was ready in 1922 for the last coping-stone. It should give great satisfaction to anyone to have built in firmly even one stone in the wall and thus to have contributed to the final success.

I turn now to the problems of research in general practice. It is heartening to see the new College of General Practitioners has already taken such an interest in this matter; and in one of their publications they have set out very clearly the present position, as follows:

> "There was a time in the history of medicine when all research was general-practitioner research, for there were none but general practitioners to undertake it. Advances were made through careful observation of one patient, or of several patients, by a doctor in practice who drew his conclusions from facts observed during the routine of a day's work. In this way Jenner recognized the relationship between cowpox and smallpox, and Withering observed the diuretic effect of the foxglove leaf. Then

came a change in the pattern of medical practice. Institutional care of serious illness and research in hospital developed on an increasing scale. The quest for more facts in the field of general practice slackened, and family doctors devoted their energies to relaying to patients the new knowledge that their hospital colleagues had gained. The flame of general-practitioner research burned low, to be fanned into occasional brilliance by such men as James Mackenzie and William Pickles. Now, once again it is being realized that opportunities to undertake research into conditions encountered in general practice are unique and wide, and that general practitioners have a duty to work on many problems which might otherwise not receive the attention and observation that they deserve."

Can the flame of research in general practice burn brightly once more? It is not easy, and very few have the real genius and will of men like Mackenzie and Pickles to do it. I knew Sir James Mackenzie well, and used to visit him in his later days at St. Andrews. I was young and actively engaged in research, and between strenuous foursomes at golf I used to argue with him. I fear I annoyed him by maintaining that the group of doctors he gathered round his institute could only carry out the observations which he himself devised and suggested, and could not begin to do real research work on their own. I think I was right, for when Mackenzie died the institute, having lost the mainspring of its activities, soon came to an end. I am glad, therefore, to see that the new College has already appointed a Research Advisory Panel of men trained in research methods to direct general-practitioner research into suitable channels.

There is a point here, based on my experience as a university professor, which is worth notice. Every good general practitioner rightly covets the higher degree of M.D., which in by far the greatest number of universities is now awarded on a thesis based on personal and original work. The word "original" must not be taken to mean too much, for, as I have explained, the firm placing of one stone alone in the wall of advancing knowledge is a fine thing to do. I am glad to say that I have more than once advised the award of an honours M.D. for work undertaken in general practice.

Nor must the general practitioner any longer consider himself at a grave disadvantage in research compared with his hospital colleagues. Medicine, as I tried to emphasize earlier in my address, still remains in many ways an observational science, and that is why the man in practice can find his problems for investigation just as easily as in a laboratory. Gregg's outstanding discovery of the effects of German measles on the unborn child during early pregnancy arose directly from simple clinical observations, and I have no doubt that ample opportunities of this kind are still ready for those who are prepared to see.

Conclusion

The advances which I have described have made modern medicine very costly—so much so that the State has been inevitably compelled to step in, with changes for our profession which we must not resent but legitimately strive to improve or modify for the benefit of all.

As the new and important methods and techniques and remedies have become available, specialism in medicine has inevitably developed, and it has come to stay. No one man can nowadays be an expert in everything, and the value of expert treatment for the patient has proved quite conclusive.

Brilliance in research and in advancing medical knowledge must, and indeed does, receive the recognition which it deserves. Fortunately, research institutes, including those devoted to clinical research, are rapidly increasing in number, and a man with the special attributes and abilities has now reasonable opportunities of devoting his whole life to medical research of many kinds.

This has created, however, a new problem in our universities and medical schools, where the future practitioners of medicine are trained in their formative years. The professor or clinical teacher, whose range as a teacher embraced most of medicine or of surgery, is gradually becoming extinct; and we must think carefully how to fit in specialists as professors and clinical teachers while still retaining a correct balance in the training. It has been said so often, and with truth, that the family doctor is now the only non-specialized member of our profession with a general but not expert knowledge of all branches of medicine. I do not regard general practice as a specialty—it is essentially the opposite.

I would claim, from my experience, that the training of our future doctors in their formative undergraduate years —and even when they return for postgraduate courses to bring their practical knowledge up to date—is an important task, the correct methods and scope of which need urgent attention in this time of change.

A broad view is required, and specialism is perhaps not the best way in which to acquire it. Men with a broad view of medical practice, derived from experience, will be urgently required in future years to steer a proper course of medical training. This must not be left to professional administrators in offices, whose tidy methods may not be the ideal ones for the practice of medicine and the best possible treatment of our patients.

The practice of medicine is now very complex, but it is our bounden duty and service to make available to our patients the very best that we know. This, I have tried to show, is a combination of the old observational skill in which we have been trained and the application of all the new and beneficial discoveries with which we have been blessed. All this makes—I am not afraid to say it—the practice of medicine a noble profession and a good life.

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The highlight of the recent annual meeting of the Royal College of Nursing was Mrs. CECIL WOODHAM-SMITH'S lecture on "Florence Nightingale—the Greatest Victorian." Miss Nightingale, she said, was very much more than just the founder of modern nursing. In two other spheres, both too little appreciated, her work had been remarkable. Although no admirer of her own sex, Florence Nightingale had made it possible—and respectable—for women from decent homes to engage in any type of work they pleased. This revolution in the status of women had not yet ended. Her second great achievement had been for the British Army. With the help of Sidney Herbert she had transformed the living conditions of the British soldier. When they started their work, the mortality among soldiers in barracks was double that in the civil population. They set themselves to improve the standards of barrack accommodation and sanitation throughout the country, and in large measure they succeeded. Then came her "culinary campaign." She agitated for ovens, drew up diet sheets, and started the first corps of army cooks, where the art of cooking for large numbers was taught. At Scutari, during the Crimean war, she had been appalled by the lack of recreational facilities for the troops. There were only the gin shops and brothels. Against strong opposition she opened a reading room for the soldiers. Many were illiterate, so she had schoolmasters sent out to teach them to read and write. Paymasters were corrupt, so she acted as the soldiers' banker to ensure that their remittances reached home. In a word, Florence Nightingale created Army Welfare.

RISK FROM THE ASPIRATION OF VOMIT DURING OBSTETRIC ANAESTHESIA

BY

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In 1937 C. C. Hall, of Oakland, California, lost a normal healthy primigravida as a result of inhalation of vomit which occurred during an anaesthesia given for a low forceps delivery. Impressed by the tragedy of the occurrence, he inquired among his colleagues in the vicinity of San Francisco and Los Angeles, and received records of 13 similar cases, 12 of which occurred within the previous two years, 4 being fatal. When publishing these cases he failed to find "a single detailed report of a similar case in the literature" (Hall, 1940). Following this, reports were published of maternal deaths due to inhalation of vomit by Eastman (1941) and Dieckmann (1945). The latter found 45 cases of aspiration of vomit occurring in 46,000 deliveries under general anaesthesia at the Chicago Lying-in Hospital. Of this number, eight patients were seriously ill and two died.

In 1946 Mendelson published a classical paper on aspiration of the stomach contents during obstetric anaesthesia in which he distinguished the asthmatic type due to aspiration of liquid gastric contents from the very different syndrome of lung collapse due to inhalation of solid material. He offered experimental evidence in rats of the part played by the irritant acid of the gastric contents in the development of the asthmatic type of lesion, and pointed out that it is almost confined to obstetric practice.

Further reports continued to appear in America from obstetricians and from anaesthetists (Gordon, 1947, 1952; Merrill and Hingson, 1951; and others). A full account of the condition now appears in the textbook by Greenhill and DeLee (1951).

In the British literature, Marshall (1947) was quick to point out the serious implication of these reports, and he emphasized the advantage of local (or even spinal) analgesia in operative deliveries performed when the patient is in labour. Willcox (1949) published two case records, and Gilliatt (1949) commented on three cases of inhaled vomit which appeared in a series of 55 maternal deaths from 23 hospitals occurring in a total of 34,146 deliveries. He stated emphatically that these were deaths "which should not have occurred," and stressed the vital importance of having an experienced anaesthetist attached to every maternity hospital of any size. Despite this, there is still little reference to the seriousness of the condition in most standard British textbooks on obstetrics or anaesthesia.

The following seven cases are presented as further evidence of the dangers which lie in wait for the obstetric patient in labour to whom an inhalational anaesthetic is administered. In each case premedication was by 1/75 or 1/100 gr. (0.87 or 0.65 mg.) of atropine sulphate.

Case 1

This patient, aged 28, had a history of two caesarean sections on account of a grossly contracted pelvis and disproportion. In her third pregnancy arrangements were made for her to have a repeat caesarean section. She was admitted in the 39th week of her pregnancy, and general anaesthesia was begun with nitrous oxide, oxygen, and ether. Inhalation of ether was followed by laryngeal spasm and temporary cyanosis. The spasm recurred, but the anaesthetic was continued and the operation proceeded. A male child weighing 7¼ lb. (3.4 kg.) was extracted, but during wound closure a severe attack of spasm and cyanosis occurred and vomit was found to be coming from the mouth. Despite artificial respiration and nikethamide the patient died before the conclusion of the operation.

Post-mortem Findings.—The body was that of an apparently healthy woman. The dilated stomach contained a large amount of semi-fluid digested food. The trachea and bronchi contained a quantity of aspirated vomitus.

Comment.—This patient was admitted at 11 a.m. on the day of operation for elective caesarean section on the following day. The operation was in fact performed 12 hours after admission because it was believed that she might be in labour, and it is probable that the patient had food after her admission.

Case 2

This woman, aged 24, was booked for trial of labour. The first stage was slow, but the cervix gradually dilated and she reached full dilatation after 36 hours, during which she received adequate sedatives. Her pulse rate was consistently below 100. During this time, in accordance with the hospital policy of encouraging the intake of fluids and glucose during labour, a total of 108 oz. (3 litres) was given by mouth. She vomited soon after admission, but there was no further vomiting. A total of 84 oz. (2.4 litres) of urine was passed. After two hours in the second stage, the patient had failed to deliver herself and the head was found to be arrested in the deep transverse position. Manual rotation and forceps delivery were carried out under general anaesthesia (nitrous oxide, oxygen, and ether) without any obstetric difficulty. During the induction and progress of anaesthesia, vomiting occurred several times, the vomit being mopped away by the anaesthetist. There was no cyanosis or obstruction of respiration and the patient gave no cause for anxiety at the time. One hour after delivery the pulse was noted to be rapid, and the patient on recovering from the anaesthetic became restless and cyanosed. Her condition improved on administration of oxygen but slight cyanosis remained. One hour later the pulse rate was 152 and the respiration rate 50. Three hours after delivery sudden collapse occurred; she became extremely restless, then the pulse became imperceptible at the wrist, and she died.

Post-mortem Findings.—The air passages were filled with mucoid fluid, but no solid vomited material was found. No further details are available.

Comment.—This case well illustrates the difficulties to be met with in a maternity unit. At the same time as this delivery was being undertaken, a breech extraction became necessary in another theatre. Two anaesthetists (one senior registrar and one trainee) were available. The anaesthesia for the forceps delivery was begun under the eye of the registrar before she went to give the other anaesthetic, which was thought to present the greater difficulty.

Case 3

This patient, aged 30, in her first pregnancy had a premature baby which failed to survive. In her second pregnancy she was admitted in labour when 39 weeks pregnant. She made steady progress, being 15 hours in the first stage of labour, but uterine contractions were poor in the second stage and a forceps delivery was undertaken when the maternal pulse began to rise. An easy extraction of a child weighing 7¼ lb. (3.4 kg.) was carried out. During induction (nitrous oxide, oxygen, and ether) a substantial amount of vomitus was expelled, but no impairment of colour resulted. The anaesthesia was continued apparently satisfactorily, and at no time did the patient give cause for

anxiety. Immediately after cessation of the anaesthesia some cyanosis of the lips and nail-beds was noted and the pulse rate was 150. One hour after delivery, despite continuous oxygen, the breathing was laboured and the cyanosis more pronounced. The patient then had two fits preceded by twitchings of the face and arms, and she died one and a half hours after delivery. Examination with a laryngoscope showed much debris in the nasopharynx, but the glottis was not obstructed.

Post-mortem Findings.—There was no vomit, blood, or foreign material in the upper respiratory tract. There was, however, a little frothy transudate from the lungs. Both pleural cavities contained several ounces of straw-coloured transudate. The lungs contained a large amount of oedematous fluid.

Case 4

A primigravida, aged 36, was admitted in labour as an emergency because of uterine inertia. A forceps delivery was undertaken after 48 hours of contractions, the head lying in the occipito-posterior position. The extraction was not easy, but a child weighing 7 lb. 3 oz. (3.3 kg.) was delivered in good condition. The anaesthetic used was nitrous oxide, oxygen, and ether. The patient was lightly anaesthetized throughout. On one occasion during manual rotation of the head she appeared to be going to vomit, but no vomitus was seen and the anaesthesia proceeded normally. Her colour remained good and at the end of the operation she showed signs of regaining consciousness. The pulse rate was 100, the respirations regular, and her colour a little cyanosed. One and a half hours after delivery the theatre sister noted: "Pulse rate 160, quality fair, colour cyanosed." The blood pressure was 96/54. Oxygen, morphine, and nikethamide were given, but there was no material improvement. Twelve hours later the pulse rate was 136 and the respiratory rate 36; the blood pressure was 96/30. The respiratory rate rose further, respiration itself became extremely laboured, and the patient died 48 hours after delivery.

Post-mortem Findings.—The mouth, larynx, and trachea showed no evidence of obstruction, but the air passages all contained frothy fluid. All lobes of the lungs showed marked oedema, rendering the whole of the lung substance airless. The pleural sacs each contained about half a pint (285 ml.) of straw-coloured fluid. The heart was normal in size and showed no obvious dilatation.

Case 5

A primigravida aged 32 was admitted in labour as an emergency on account of a prolonged first stage. On admission her urine contained a large amount of acetone and she received 1,000 ml. of intravenous glucose, 5% solution. The cervix at this stage was three-quarters dilated. Eight hours later it was fully dilated and forceps delivery was undertaken for maternal distress after one hour in the second stage. A child of 7 lb. 13 oz. (3.5 kg.) was extracted satisfactorily. The patient's condition was reported as "good" at the end of the operation. No specific note concerning the anaesthetic (nitrous oxide, oxygen, and ether) was made. Two hours after delivery the theatre sister noted: "Pulse imperceptible, colour extremely cyanosed, coughing up fair amount of mucus." Nikethamide was given. Two hours later the patient was conscious and the colour somewhat better, but the pulse rate was 136 and the respiratory rate 44. She received plasma, penicillin, morphine, and oxygen, but the pulse rate never fell below 120 or the respiratory rate below 28, and 36 hours after delivery she became severely cyanosed and died.

Post-mortem Findings.—Massive oedema of all lobes of the lungs, the substance of the lungs being completely sodden. The stomach was greatly distended and contained thin, blackish fluid. There were small flecks of black material adherent to the mucous membranes of the trachea. The right side of the heart was considerably dilated. The cause of death was given as "massive pulmonary oedema, cardiac failure, inspiration of vomit, and dilatation of the stomach."

Comment.—In this case it seems that the incident of aspiration completely escaped the notice of the operator and anaesthetist; certainly no note of any difficulty was recorded.

Case 6

An infertile primigravida aged 34 was admitted at the 39th week of her pregnancy with early rupture of the membranes. Contractions began soon after admission, and after nine hours she became fully dilated. Delay in the second stage of labour was associated with a posterior position of the occiput, and after two hours she was delivered by Kielland's forceps. The anaesthetic used was nitrous oxide, oxygen, and ether. A note was made that vomiting occurred during the induction of anaesthesia and was followed by troublesome coughing. The pulse rate after delivery was 116 and remained at that rate for two and a half hours, but there was no cause for anxiety. Three hours after delivery the theatre sister's notes read: "Colour cyanosed, coughing thick mucus. Respiration distressed." After the administration of morphine, ¼ gr. (11 mg.), and oxygen the patient's colour improved, but she continued to cough up thick mucus.

A summary of the notes of a general physician who was asked to see her reads: "Dyspnoea, cyanosis, tachycardia, productive cough. Signs of partial collapse of both lower lobes, particularly the right. Bronchoscopy under local analgesia—much sticky secretion aspirated but no single bronchial block seen." This was performed nine hours after delivery and by the following day her pulse rate had come down to 86. Her breathing, though embarrassed, was not troublesome, but there were plentiful rales over both lungs. She made a good recovery, the chest being free from adventitious signs at the end of a week.

Case 7

This patient, aged 30, was booked for a trial of labour in her second pregnancy on account of a contracted pelvis. Her first child had been a stillborn hydrocephalic. Labour began spontaneously, and after 15 hours in the first stage and one hour in the second manual rotation and forceps delivery were undertaken for deep transverse arrest of the head. Anaesthesia was complicated by vomiting during the induction. The pharynx was cleared by suction with a mechanical pump and the anaesthesia continued smoothly. The patient recovered consciousness soon after completion of the delivery and spoke to the nursing staff.

One and a quarter hours after delivery she became cyanosed. The pulse rate rose to 150 and the respiration rate to 44. The blood pressure was 115/60. On listening to the chest, scattered moist sounds could be heard on both sides, but there was no evidence of collapse. It was difficult to relieve the cyanosis by the use of oxygen, and one hour later she became very restless and was given paraldehyde intramuscularly. Three hours after delivery the pulse was still very rapid but the colour was much improved. Oxygen was administered continuously. The blood pressure was 98/80. The patient herself appeared quite unconscious and her breathing was extremely laboured. It was noted that the chest failed to relax in expiration, and it was difficult to maintain full oxygenation. Digoxin and methedrine were given, and she improved gradually over the next 12 hours. At that time the pulse was 124 and respiration rate 28. She was removed from the oxygen tent after 48 hours and thereafter made a good recovery. The day after delivery she complained of low sternal pain, and two days later was coughing a rusty sputum. *X*-ray examination of the chest on the fourth day (Fig. 1) showed oedema of the upper and lower lobes, which had cleared almost entirely by the 14th day (Fig. 2).

Incidence

The above cases were all patients at the Birmingham Maternity Hospital. This hospital books only abnormal or potentially abnormal cases for delivery, and, in addition, accepts a high percentage of emergencies (up to 50% in the earlier years covered by this report). In such a highly

selected group any figures of incidence are of little value and therefore no detailed analysis is presented. During the 10-year period 1943–52, 18,524 cases were delivered in the hospital; 99 maternal deaths occurred, and, of these, five (Cases 1 to 5) are regarded as attributable to aspiration of vomitus under anaesthesia. In a further two or three cases it is felt in retrospect that death may have been due to the syndrome reported here, but the records refer to "left ventricular failure," "obstetric shock," and post-mortem examination was refused. Gordon (1952), in a review of maternal deaths, shows that the recorded cause of death is not always an absolutely reliable estimate.

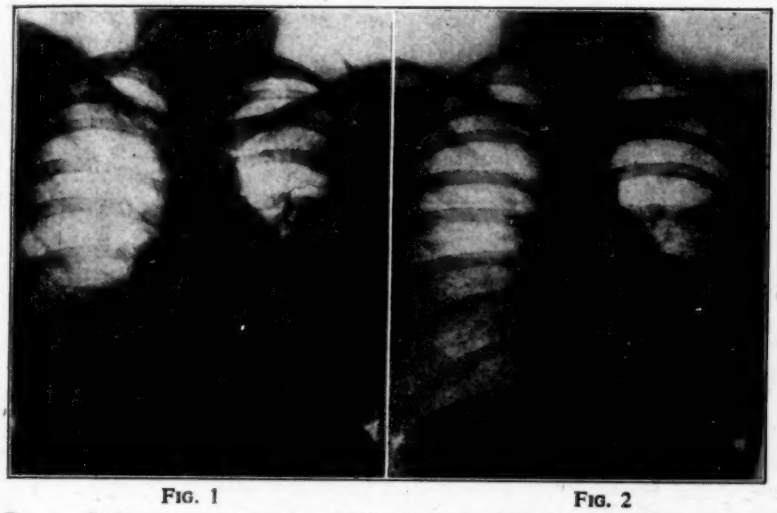

FIG. 1 FIG. 2

FIG. 1.—Radiograph of Case 7, showing oedema of left upper and lower lobes, mainly peripheral in distribution. FIG. 2.—Radiograph of same case, showing left lung fields to be almost clear.

Two non-fatal cases (Nos. 6 and 7) are recorded here as examples of serious illness resulting from the same cause. Many other cases showing minor degrees of the "acid aspiration syndrome" occurred, but it is not possible to trace all, and no figure for the incidence of the condition in this hospital can be given. Hartzell and Mininger (1946) recorded 20 cases of "broncho-pneumonia" following ether anaesthesia in obstetric patients which they believed to be due to aspiration of vomit, but of their cases only one required bronchoscopy and none was seriously ill. This would seem to confirm that less severe examples of the condition are not uncommon.

Labour Ward Management

In general the policy of the hospital is to permit no solid food in labour. To combat exhaustion and acidosis the mother is encouraged to take fluids and glucose in the first stage of labour. Intravenous dextrose solution is used only in the treatment of established acidosis.

Caesarean section is performed on a surgical operating table. All other deliveries are performed on labour beds, which can be tilted laboriously by hand, but which cannot be dropped into the Trendelenburg position.

During the years under consideration a large majority of the operative deliveries were carried out under general inhalational anaesthesia. From 400 to 500 anaesthetics per annum were given to patients for delivery, most of whom were in labour. Local and spinal analgesics were occasionally used, but together they accounted for less than 10% of cases. Most anaesthetics have consisted of nitrous oxide, oxygen, and ether, but some variations from this routine have taken place in later years. No relaxants were used in the cases under review.

Clinical Features

Case 1 illustrates the obstructive type of lesion in which inhalation of solid or partially digested food causes acute asphyxia and, in severe cases, death from acute heart failure. This type of case is familiar also to those engaged in emergency surgery. Its treatment consists in removal of inhaled material at the earliest possible moment. The remaining cases illustrate the asthmatic type of lesion as described by Mendelson (1946).

The inhalation of a minimal amount of liquid stomach content in the conscious subject will result in intense laryngospasm and an irritant tracheitis which give rise to violent cough, obstruction to the intake of air, and sometimes substernal pain. Such a condition, if it occurs during the phase of recovery from an anaesthetic, may give rise to some alarm, but recovery is usually rapid. The patient's protective reflexes will prevent more than a small amount of liquid from being aspirated.

Cases 2 to 7 illustrate a much more serious clinical picture than this, and a study of these cases in conjunction with those of Hall (1940) suggests that the seriously ill and fatal cases have all been in the group who vomited during the *induction* of the anaesthesia as opposed to the recovery phase. On continuing the anaesthetic, the patient's condition in each case became satisfactory for a time. No anxiety was felt at the conclusion of the operation in several cases, and the surgeon and anaesthetist had on these occasions left the theatre when, after an interval of one to two hours, tachycardia, tachypnoea, and cyanosis developed. In such cases cyanosis is commonly relieved, but not completely banished, by the administration of oxygen. Breathing is laboured and the chest fails to relax during expiration. Widespread adventitious sounds are heard all over the chest, but there is no large area of collapse. If the cyanosis is not relieved, respiration becomes increasingly distressed, and the accessory muscles of respiration are active. This stage is critical. Cerebral anoxia may lead to extreme violence, sometimes maniacal, and the combination of prolonged asphyxia and exhaustion will lead to heart failure, generalized pulmonary oedema, and death.

Causes and Effects of Aspiration

The "asthmatic" lesion due to inhalation of liquid vomit is much commoner in obstetrics than asphyxia from aspiration of solid or semi-solid food. It is almost peculiar to obstetric cases for the following reasons. It is agreed by all clinical observers that the emptying time of the stomach in labour is considerably prolonged. Yet the consumption of liquid is often encouraged. It is not surprising, therefore, that large amounts of fluid can accumulate in the stomach during labour. With the patient lying flat, regurgitation of stomach contents can occur with exceptional ease, almost silently, without warning retching, and it can be readily induced by changing to the lithotomy position or by the application of fundal pressure during anaesthesia. If, as seems probable, the condition is commoner in patients delivered by forceps than in those undergoing caesarean section, the explanation may depend in part upon the tendency to perform the former with the patient flat and the latter with a slight head-down tilt. Further, the restriction of premedication to atropine only and the diminished respiratory excursion of a patient at term may make the induction of anaesthesia unusually difficult.

The following hypothesis is therefore proposed: when liquid inhalation occurs during the *induction* of anaesthesia the patient with reflexes partially inhibited may not readily expel the irritant fluid. If removal by coughing or suction is not complete when the anaesthesia is recommenced and deepened, the inspired vomit is free to spread further into the air passages.

The precise pathological lesion present in the individual will vary with the amount and character of the matter inhaled (whether solid or liquid) and with the duration of the exposure to the foreign matter. A tracheitis is the slightest lesion which will result from aspiration. Further extension

of the irritant liquid down the respiratory tree will result in contamination of the bronchi, bronchioles, and even the alveoli of certain areas of the lung field. This, however, may have little immediate effect on pulmonary efficiency, since much of the total lung area is unaffected and this is confirmed by the satisfactory state of patients 2 to 7 while they remained under the effects of the anaesthetic. When consciousness returns spasm of the smaller bronchi in the affected zone of the lungs, already oedematous from acid contamination, may result in local areas of collapse; small particles of food may produce the same effect by blocking individual bronchioles.

Yet these local changes should not of themselves prove fatal, and it is suggested that danger to life in the "acid-aspiration syndrome" arises with the development of a *generalized* bronchospasm which may come about when the effects of the anaesthetic have disappeared. This would explain the interval commonly recorded between the end of the anaesthesia and the onset of serious symptoms. (The delay could equally be due to the time necessary for widespread obstructive oedema to develop in the air passages, but post-mortem examination has not supported this in our cases.) Pulmonary gas exchange is gravely impaired by the generalized bronchospasm, and cyanosis develops. At the same time the strenuous respiratory efforts which attempt to overcome the bronchiolar constriction result in diminished intra-alveolar pressure. This may be the mechanism by which widespread pulmonary oedema begins. If anoxaemia persists then heart failure results, massive pulmonary oedema develops, and death occurs.

At post-mortem examination gross pulmonary oedema is the outstanding finding. On squeezing the lung, liquid pours out as from a sponge. The underlying lung lesion is thereby obscured, but the area of lung originally involved by aspiration can be clearly recognized by radiography in those patients who recover (see Fig. 1).

Prevention

In considering the prevention of this serious maternal risk it is necessary first to examine the possibility of using alternative methods of anaesthesia free from the danger of aspiration, and, secondly, to propose measures to reduce the chances of mishap where inhalational anaesthesia is the method of choice.

Choice of Anaesthesia

Inhalational Anaesthesia.—Hingson and Hellman (1951) analysed 330 maternal deaths resulting from anaesthesia and found aspiration of vomitus responsible for 155, the second most frequent cause being "overdosage of spinal anaesthesia" (24 deaths). As the total number of each form of anaesthetic administered from which their series is drawn is not stated, the implication of the figures may be quite erroneous, but our observations confirm their belief that inhalational anaesthesia is not free from danger. In all the cases reported here the anaesthetic has consisted of nitrous oxide, oxygen, and ether administered through a standard Boyle machine. There is no firm opinion concerning the safest technique, agent, or combination of agents for anaesthesia during labour, although ether has always had the reputation of possessing the widest margin of safety. Yet Merrill and Hingson (1951), reporting 59 such maternal deaths, found that two out of three deaths occurred when ether was used, either alone or with nitrous oxide. No death occurred with chloroform or local or caudal anaesthesia, but the total number of each type of anaesthetic given in the series is not stated, and it would be unwise to draw conclusions about the relative safety of different methods. It would seem, however, that there is a place for further investigation into the comparative safety of available inhalational anaesthetics in labour: for example, it has been said that this type of fatality is rarely or never encountered in domiciliary midwifery, where the open-drop method of anaesthesia is usual; if this be true, it is possible that the positive pressure of gases in a semi-closed apparatus may be a factor in promoting aspiration.

Spinal anaesthesia in obstetrics is championed by some authors, including Thomas (1947), Rawlings (1950), and Thorne (1952), who report personal series without mortality in caesarean section and operative vaginal deliveries. It has occasionally been used in the past by obstetricians who preferred it, with its hazards, to the unskilled general anaesthetic of the obstetric house-surgeon. The safety of the method has been increased in recent years. Improvement began with the campaign for absolute sterility advocating the use of dry autoclaved instruments and condemning the habit of rinsing in "sterile" water and the use of labelled ampoules (sometimes faulty) kept in antiseptic solutions. Recent writings have drawn attention to the usefulness of drugs, such as methyl-amphetamine, which combat sudden drops in blood pressure and have emphasized the necessity of giving oxygen in view of the diminished respiratory excursion at term. With these precautions Macintosh (1950) gives the method his approval. Nevertheless, spinal anaesthesia is open to grave objections. Greenhill (1951) quotes an estimated incidence of 0.25% of grave spinal-cord paralyses, and rightly mentions the ever-present risk of purulent meningitis. Because of this he is strongly opposed to it.

Epidural, Caudal, and Paravertebral Block Anaesthesia.—All these appear to give a wide margin of safety, but as yet have technical difficulties which place them beyond the scope of common use in a busy hospital; from lack of experience no comment can be made upon their usage here.

Local Analgesia.—For the present this is the safest method available and the method of choice wherever it can be used. In our hands it has not always been successful in abolishing pain, but the introduction of hyaluronidase has been of great assistance, and Greenhill (1951) considers xylocaine to be a further advance in infiltration anaesthesia. He states that its power of diffusion is such that accurate anatomical pin-pointing of nerves is no longer essential.

Summarizing, local analgesia is the safest of the common methods available. When its use is not permissible and if the patient is not in labour, general anaesthesia will probably be the method of choice, as the risks of inhalation are then minimal. When the patient is in labour the merits of spinal as opposed to general anaesthesia should be given due consideration, but the final choice must be an individual one, depending upon many factors, including the wishes of the patient and the experience of the anaesthetist.

Prevention of Vomiting

In the past much emphasis was laid on maintaining the nutrition of the patient. While solid foods have usually been forbidden in labour, intake of glucose and of fluids has often been encouraged (this can be seen from the records of Case 2). If local or spinal anaesthesia is the method to be employed in the event of operative delivery being necessary, no change from this plan is required, but in hospitals where general anaesthesia is used for delivery many authors now insist that intake by mouth be reduced to a minimum, maintaining that if acidosis develops treatment should be by intravenous administration of dextrose (500 to 1,000 ml. of 10% or 5% solution, given as required). If it is desired to maintain the policy of giving water and glucose liberally in labour the only real safeguard for the patient due to have a general anaesthetic is to empty the stomach through a wide-bore stomach tube. If this unpleasant procedure be omitted (at the discretion of the anaesthetist) the following conditions should be satisfied: (*a*) an experienced anaesthetist to be in charge of the case; (*b*) operation to be performed on an operating table where tilting of the patient can be performed within seconds; (*c*) an efficient mechanical sucker to be available for the anaesthetist's use; (*d*) a laryngoscope and bronchoscope to be ready at hand.

Mendelson also recommends a transparent face-piece. The use of Clauson's harness is widely condemned in these cases. In some cases there is obviously an advantage in the use of a cuffed intratracheal tube, if this is possible.

Treatment

Where vomiting occurs during the induction of anaesthesia, the anaesthetist, appreciating the danger of the situation, will encourage the patient, by tilting and suction, to get rid of all vomitus, and the decision to continue with the anaesthetic will be left to his judgment that no aspiration has occurred. If asphyxia develops, solid vomit may have been inhaled. Immediate endoscopy is then indicated for removal of the foreign material. Merrill and Hingson (1951) describe a case in which tracheotomy was required for the removal from the trachea of leaves of spinach, eaten 18 hours before.

When, despite precautions, respiratory spasm develops on recovery from the anaesthetic, treatment should be given along the following lines:

1. If not already performed, bronchoscopy should be undertaken, since the presence of solid debris in the air passages cannot otherwise be excluded. In order to do this it is suggested that the patient should be re-anaesthetized. If it be true that spasm is the main cause of the cyanosis, this measure alone should restore the patient to a satisfactory condition. Through the bronchoscope a suction tube should be passed well down the respiratory tree.

2. The use of oxygen is obviously essential, and it might be found advantageous to combine it with helium in a ratio of helium:oxygen, 70:30.

3. Antispasmodics should be given—intravenous aminophylline or adrenaline will be the first choice, but intravenous A.C.T.H. might be tried in the light of reported success in the treatment of status asthmaticus.

4. If the patient improves on being re-anaesthetized and deteriorates on regaining consciousness, the possibility of maintaining her under anaesthesia for a further period of time should be considered.

Summary

Six cases, four fatal, of the "acid aspiration syndrome" following inhalational anaesthesia in obstetrics are described, together with one case who died from inhalation of solid vomit.

The grave examples of the syndrome generally follow vomiting during the *induction* of anaesthesia, and a hypothesis is proposed to explain this.

No single method of anaesthesia is adequate for all obstetric cases, but a plea for the wider use of local analgesia is advanced.

In inhalational anaesthesia the importance of the stomach tube, a tilting table, and a mechanical sucker are emphasized in the prevention of disaster. The passage of a bronchoscope is regarded as a first essential in the treatment of the established condition. It is suggested that benefit may come from recommencing the anaesthetic in order to do this.

I wish to thank the consultant staff of the Birmingham Maternity Hospital for permission to publish case records of patients in their care and for much helpful advice in the preparation of this report.

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BODY WEIGHT AFTER GASTRECTOMY

BY

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Patients who have undergone subtotal gastric resection often show subsequent loss of weight. Muir (1949) considered weight loss to be second to the "dumping syndrome" as a cause of dissatisfaction with the result of operation, and found that 40% of his patients had lost 7 lb. (3.2 kg.) in weight six months afterwards. Wells and Welbourn (1951) estimated that on the average their patients had lost 17 lb. (7.7 kg.) from their best or pre-illness weight before operation, and that they registered an average gain of 3 lb. (1.4 kg.) after it. Such loss of weight was mainly seen in patients who had previously maintained their weight fairly well: thus in those whose pre-operative weight was within 14 lb. (6.4 kg.) of their best weight there was an average loss after surgery of 7 lb., whilst in those who had lost more than 14 lb. before operation there was an average gain of 18 lb. (8.2 kg.) subsequently.

The use of the best or "pre-illness" weight as a yardstick is open to the objection that it is often wrongly estimated and that it is not possible to distinguish between those patients who were once considerably overweight and those who, while still in normal health, weighed relatively little considering their age and height. This difficulty can be overcome by relating the pre-operative and post-operative weights for each individual to the standard weight for the appropriate sex, height, and age. Though Wells and Welbourn state that the body weight is stabilized by one year after operation, there are no available data showing when loss of weight occurs, and whether it is a sudden or a gradual process.

Wollaeger *et al.* (1946) stated that impaired fat absorption is found in patients who have lost weight after gastrectomy, and Muir (1949) noted the presence of steatorrhoea in five out of seven underweight patients. Wells and Welbourn suggested that the steatorrhoea was due to small-intestinal "hurry," and Brain and Stammers (1951), reporting the condition after total gastrectomy, attributed it to a faulty admixture of food with bile as a result of "dumping" of food into the jejunum. These authors also found that fat absorption is better when the diet has a high fat content than when this is low. These studies have been made on small numbers of selected patients, and no control experiments are reported. Attempts to increase fat absorption by increasing the dietary fat (Brain and Stammers, 1951) and by the use of emulsifying agents (Badenoch *et al.*, 1951) have met with little success in producing a gain in weight.

Methods and Material

The observations reported here have been made upon 285 patients submitted to subtotal gastrectomy for peptic ulcer at St. George's Hospital, all of whom have been personally followed from the time of operation for at least one year. A gastro-jejunal anastomosis was carried out in 225 patients, and a Billroth I operation of comparable extent in 60. The problem of body weight after operation has been studied in the following way.

1. The weight of each patient has been related to the standard figure for sex, height, and age, and expressed as a percentage of this figure. Weight has been studied immediately before operation, on discharge from hospital, and at two, six, and twelve months after operation. The

standard weight is the mean weight of individuals of given sex, age, and height based on observations of 28,697 persons in the practice of seven British life assurance companies. The figures were obtained before the war, and it is appreciated that dietary and other changes since then may have affected their absolute accuracy. As a working standard of comparison their usefulness is unimpaired, and the only modern figures obtainable are all from American sources.

2. Five-day fat-balance studies have been carried out as follows : (*a*) upon nine patients immediately before the performance of gastrectomy, and again one month after operation ; (*b*) upon five patients immediately before and one month after surgical operations other than gastrectomy (prostatectomy, hernioplasty, splenectomy, appendicectomy) ; and (*c*) upon 11 patients one year after gastrectomy, five of whom had lost 20% or more of standard weight while six had maintained or gained weight. The daily fat intake during the balance period was 50 g. The faecal fat was estimated after ether extraction of the dried stool by the Soxhlet method.

3. The gastric emptying rate and small-intestine transit time have been studied after administration of a barium meal in 128 patients who had undergone gastrectomy. Eighteen of these patients had lost 15% or more of standard weight following operation. The small-intestine transit time was judged by the position of the head of the meal two hours after ingestion.

4. Intensive early post-operative feeding has been employed in 12 patients weighing between 80 and 90% of standard before operation, and they have been followed for six months afterwards. The method used has been drip feeding by a tube placed in the jejunum at the time of operation (Stengel and Ravdin, 1939) or by gastric tube. Feeding was started on the third morning after operation, provided that good bowel sounds were present, and the following mixture was used : "casilan," 200 g. ; sucrose, 200 g. ; arachis oil, 100 ml. ; whole milk, 1,500 ml. ; sodium chloride, 5 g. ; ascorbic acid, 1,500 mg. ; water to 3,000 ml. This gives a daily intake of 36.7 g. of nitrogen and 3,420 calories. Further fluid up to 1,000 ml. daily was taken by mouth as desired. Mouth feeding began on the sixth day, and was supplemented by the drip to keep the daily calories and nitrogen intake constant. The tube was removed on the morning of the tenth day, and frequent feeds were given to ensure a daily intake of at least 2,800 calories.

Results

1. Body Weight Before and After Operation

The body weight of each patient has been expressed as a percentage of his standard weight, and the series has been divided into groups according to the deviation from standard weight present before operation. For convenience of presentation the groups are made up in terms of 10% variations from the standard, and Fig. 1 shows the numerical distribution in these groups, before operation, of the patients in the series. It is apparent that more than 75% of patients are under standard weight at this time.

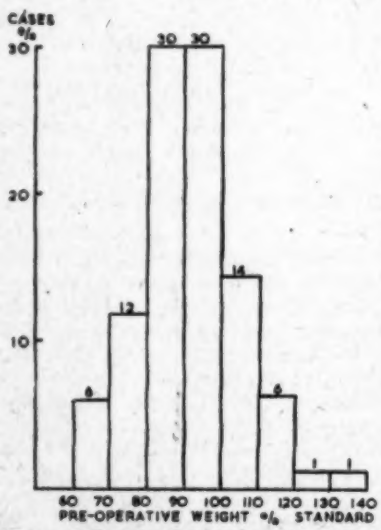

FIG. 1.—Weight distribution of patients before operation.

Table I compares the distribution of patients before operation with that one year afterwards. To avoid a misleading impression being produced as a result of small changes in weight, a change in group is only shown if the change in weight is greater than 5% of standard. Over the whole series this gives a reliable picture of what is happening, and three examples illustrate the changes in different groups. In the group of 43 patients weighing 100–110% standard before operation, 25 were in the same group, 12 in the group 90–100%, and 6 in the group 80–90% one year afterwards. Of 84 patients originally 80–90% standard, 11 were in a higher group at one year, 50 remained in the same group, and 23 were in a lower one. Sixteen patients were grossly underweight at the time of operation (60–70% standard), and, of these, 11 attained a higher group and 5 remained in the same one. Thus after operation there is a definite downward shift in the weight of 25–30% of patients in all the pre-operative groups except the lowest. It is also apparent that the greatest loss of weight occurs in the patients in the higher groups, though the result from an individual point of view is the same for the patient who has failed to gain on a pre-operative weight of, say, 70% of standard as it is for another who reaches the same level only after a frank post-operative loss of many pounds.

TABLE I.—*Showing by Groups the Change in Weight Distribution One Year After Operation*

Weight as % Standard	No. of Cases	
	Before Operation	1 Year After Operation
140–130	3	1
130–120	3	2
120–110	16	8
110–100	43	49
90–100	83	77
80–90	84	79
70–80	37	60
60–70	16	9

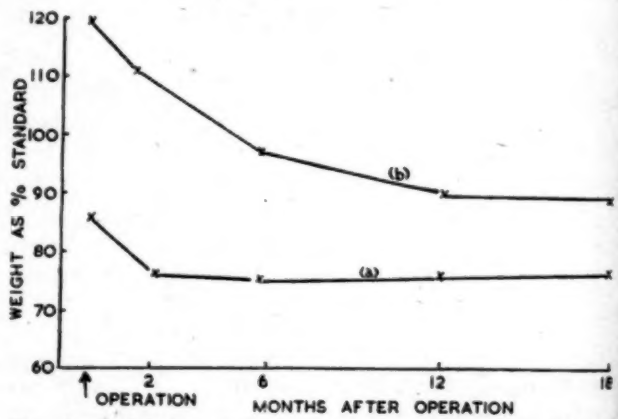

FIG. 2.—Weight-loss patterns after gastrectomy. (*a*) Average curve for 23 patients originally weighing 80–90% standard. (*b*) Curve for one originally overweight patient.

The weights of 23 patients in the pre-operative group 80–90% who subsequently were in a lower group have been recorded at two, six, and twelve months after operation. Almost all the weight loss occurred in the first two months, and after that time only minor fluctuations in weight took place, often in the form of slight gains (Fig. 2). These patients therefore subsequently *fail to gain* upon a low weight which has been established at the end of convalescence. In the lowest groups a corresponding deviation from standard weight is already present before operation, though, even so, some further loss may occur soon afterwards. The progressive loss of weight reported after total gastrectomy is rare after less extensive resections, except in patients who are considerably over standard weight before operation. The pattern of weight loss in these patients is different from that just described, and weight may gradually be lost over a period of twelve or even eighteen months. Though many pounds may be lost, the weight nearly always stabilizes ultimately within 10% of the standard figure.

2. Fat Absorption After Gastrectomy

Table II shows the fat-absorption figures in the nine patients before and after gastrectomy, and in five before and after other operations. Diminished absorption does occur in every case after gastrectomy, but the drop as a rule is small (average 4%), and is close to the experimental error of the method. After other operations a 3% drop was found in two cases, and there was scarcely any change in the other three. Absorption of 80% or less was found in one of the controlled gastrectomy cases and in three of the eleven uncontrolled cases studied one year after operation. In Fig. 3 the weight one year after operation is shown plotted against the fat-absorption figures for all the 20 patients studied. They have been divided into two groups on the basis of their daily calorie intake—those with a daily intake of more than 2,700 calories and those with an intake of less than 2,500. It is apparent that weight is related to calorie intake and to fat absorption. Both the high-calorie and the low-calorie group had the same relation between weight and fat absorption.

TABLE II.—*Fat Absorption (5-Day Balance) Before and One Month After Gastrectomy in Nine Patients and in Five Patients Undergoing Different Operations*

Operation	Fat Absorption	
	Pre-operative	Post-operative
Gastrectomy	90%	83%
"	93%	89%
"	93%	90%
"	89%	86%
"	95%	91%
"	93%	90%
"	88%	86%
"	93%	91%
"	84%	75%
Prostatectomy	91%	92%
Appendicectomy	93%	90%
Prostatectomy	88%	89%
Hernioplasty	89%	88%
Splenectomy	92%	89%

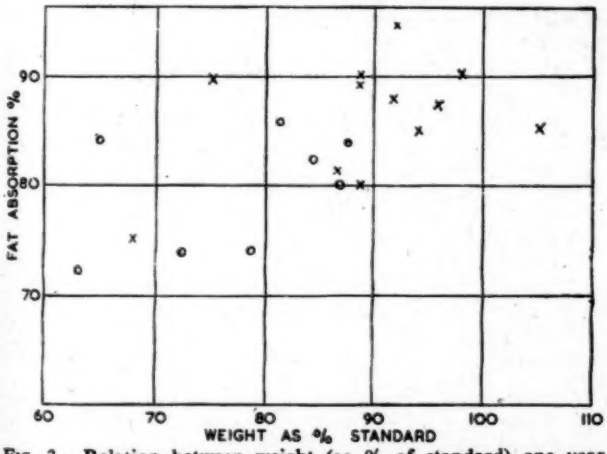

FIG. 3.—Relation between weight (as % of standard) one year after operation and fat absorption. O = Patients with daily calorie intake less than 2,500 calories. X = Patients with daily calorie intake greater than 2,700 calories.

3. Radiological Studies

Table III shows the relation between the gastric emptying rate and the small-intestine transit time in 110 cases after gastrectomy. The transit time is clearly independent of the rate of emptying time of the remnant, and hurry is not initiated by a "dumping" of the gastric contents into the small intestine. The gastric emptying rate and small-intestine transit times for 18 patients who had lost 15% or more from standard weight after operation are shown in Table IV.

TABLE III.—*Gastric Emptying and Small-intestine Transit Times in 110 Patients Following Gastrectomy*

Gastric Emptying Time	Intestinal Transit: Position of Barium Meal at 2 Hours		
	All Small Gut	½ Small Gut / ½ Large Gut	All Large Gut
X-ray dumping	12	3	0
10–20 minutes	18	0	0
Over 20 minutes	70	5	2

TABLE IV.—*Gastric Emptying Rate and Small-intestinal Transit Time in 18 Patients who had Lost 15% or More of Standard Weight Following Operation*

Loss after operation as % Standard Weight	Gastric Emptying Time	Intestinal Transit
15	Slow–normal	Normal
17	Normal	"
20	"	"
23	"	"
15	Rapid	"
18	Normal	"
18	"	"
20	"	"
15	"	"
20	"	Very fast
20	"	Normal
15	Dumping	"
15	Normal	"
17	Dumping	"
21	Normal	"
20	"	"
15	Dumping	"
19	Normal	"

Gastric emptying time: normal = 20–30 minutes; slow–normal = 40 minutes; rapid = 10 minutes.
Intestinal transit: normal = head of meal in terminal ileum or at ileo-caecal valve at 2 hours.

The incidence of different rates is the same as in the large series above, and there is no evidence that the small-intestine transit time bears any relation to post-operative loss of weight.

4. Intensive Early Feeding

The weights in relation to standard of the 12 patients intensively fed after operation are shown in Table V, before and at two weeks and two and six months after operation. All the patients gained weight while in hospital, and 10 of them maintained this weight or showed a further gain at six months. Two patients could not be induced to eat an adequate diet after they went out, and both lost ground, the weight of one falling below the pre-operative level.

TABLE V.—*Body Weight Before Operation and at 14 Days, Two Months, and Six Months After Operation in 12 Patients Receiving Intensive Early Feeding*

Sex	Age	Ht. (in.)	St. Wt. (lb.)	Pre-op. Wt. (lb.)	%	After Operation			%	Shift
						14 days (lb.)	2/12 (lb.)	6/12 (lb.)		
M.	33	67	146	121	82·8	124	128	135	92·5	+9·7%
M.	42	69	160	138	86·2	143	145	150	93·7	+7·5%
M.	49	72	178	150	84·2	151	150	150	84·2	No change
M.	43	68	157	128	81·5	135	132	125	79·6	—1·9
M.	37	65	142	125	88·0	139	135	145	102·1	+14·1
M.	32	65	139	120	86·3	121	122	124	89·2	+2·9
M.	45	63	138	115	83·3	117	122	128	92·0	+8·7
M.	53	68	161	139	86·3	142	143	145	90·0	+3·7
F.	60	63	130	110	83·9	112	115	118	90·7	+6·8
F.	56	66	141	119	84·3	124	126	134	95·0	+11·3
M.	59	69	167	138	82·6	140	142	150	89·8	+7·2
M.	38	70	161	135	83·8	137	138	138	85·7	+1·9

Discussion

Many, if not the majority, of the patients who complain of being underweight after gastrectomy have no troublesome symptoms, are working, and, apart from some quantitative restriction of their diet, are leading normal lives. Though the significance of weight loss may thus easily be unduly magnified in the majority, there are some cases in which it is more often underestimated. Four different groups of patients complaining of weight loss are: (1) Those who have failed to reach some arbitrary weight which they consider proper, but in whom no loss of weight has really occurred. (2) Those few who were well above standard weight before operation and who afterwards lost a considerable amount of weight but ended up within 10% of the standard figure. (3) Those who were under standard weight

before operation and lost some more after it, but stabilized their weight at a figure 80% or better of standard and in other respects had a good or fair clinical result. (4) A group persistently remaining between 60% and 80% of standard weight after operation. There were 69 such patients in this series. Thirty of them were in higher groups before operation. The remainder were in the 60–80% groups before operation, and either failed to gain or actually lost a little more weight after it.

This last post-operative group contains a very high portion of the unsatisfactory clinical results in the series. Two years after operation eight patients in the series were regarded as being as disabled as they were before it, by reason of severe postprandial distress and fatigue. Seven of these patients are in this post-operative group. Muir (1949) and Brain and Stammers (1951) drew attention to the correlation between low body weight and restriction of the diet as a result of continued gastric symptoms after operation, and these patients illustrate this. What is remarkable, however, is that six of these seven patients were in the same low-weight category before they were operated upon—a category which includes only 53 out of the 285 patients in the series. They all suffered from the type of postprandial distress variously termed the "general syndrome" (Butler and Capper, 1951) or vasomotor "dumping syndrome" (Custer *et al.*, 1946). In all, 15 patients were at one time afflicted with this disturbance, and no fewer than 10 of them were in this small group of patients 60–80% of standard weight before operation.

The great majority of patients remaining underweight after gastrectomy lose weight either before operation or in the first few weeks after it, sometimes during both periods, and subsequently fail to gain weight from their new baseline. This study reveals that impaired fat absorption is a frequent sequel of gastrectomy, but the importance of this in determining failure to gain weight remains doubtful. Both dietary calorie intake and fat absorption are related to body weight, and failure to gain is most pronounced when both are impaired. The impression—it cannot be put more strongly—is that of the two factors calorie intake is the more important.

The problem of putting on flesh after severe weight loss has been studied from many points of view in recent years. Keys (1946) made a study of the conditions obtaining after experimental starvation in man, and Murray (1947) and Widdowson and McCance (1951) have given detailed reports upon the recovery of body weight in undernourished Germans at the end of the war. The latter authors report 19 cases in which the weights varied between 100% and 71% of standard, with an average of 82.7%; when allowed access to unlimited food the subjects consumed a diet containing 200 g. of protein and 210 g. of fat, and comprising 6,000 calories daily, and required six weeks on this intake to reach an average of 98% of standard. It is clear from these and other observations (Widdowson and Thrussel, 1951; Murray, 1947) that to register a gain in weight up to normal when starting from 80% of this or less requires a very high daily calorie, nitrogen, and fat intake. In this series of gastrectomy patients the average daily intake of 30 patients who had lost 10% of standard after operation was 2,800 calories at one year and considerably less in the first two months.

The critical period as regards body weight is the post-operative convalescent period, for it is during this period of restricted diet that the new weight "baseline" is established. The early post-operative days are further distinguished by the occurrence of negative nitrogen balance. Wilkinson *et al.* (1950) found that after gastrectomy this catabolic phase started usually on the second day and ended between the eighth and tenth days. The intravenous administration of protein hydrolysates merely resulted in an increase in urinary nitrogen excretion. Nasal tube feeding with a mixture containing 10 g. of nitrogen and 1,800 calories daily was tried in six cases, and, though a negative nitrogen balance still followed, it was shorter in duration and much less severe. The daily nitrogen intake and the calorie value of the diet for these patients are, however, small when compared with the needs reported in other conditions involving nitrogen loss.

Levenson *et al.* (1945) found that even in mild burns 125 g. of protein and 2,800 calories daily were needed to prevent progressive weight loss, and that severe cases required up to 400 g. of protein and 4,000 calories daily to reverse the negative nitrogen balance and prevent loss of weight. Similar findings are reported by Taylor (1944). Riegel *et al.* (1947) were able to keep two-thirds of a series of patients in positive nitrogen balance after operation (including gastrectomy) by giving feeds containing 0.3 g. of nitrogen and 30 calories per kg. body weight daily by intragastric or intrajejunal drip. Their findings were in agreement with those of Co Tui *et al.* (1944a, 1944b). Werner (1947) also drew attention to the necessity for a high calorie intake to spare nitrogen, and Werner *et al.* (1949) found that after surgical operation there was no loss of nitrogen beyond that observed on the same calorie intake before operation. He concluded that the post-operative nitrogen loss could be explained in terms of simple lack of calories, and that there was no evidence of abnormal mechanisms handling nitrogen metabolism after operation.

Metabolic studies were not carried out on the 12 patients reported here who were intensively fed by nasal tube during the first ten post-operative days, but their progress supports the view that weight loss can be largely prevented by high nitrogen and high calorie intake during this period. All of them gained weight while in hospital, and 10 maintained this improvement or gained further afterwards. Two lost ground after they went out, because they could not manage an adequate dietary intake. Thus by intensive early feeding a patient may be returned to his normal environment without any additional weight deficit, acquired in hospital, to wipe off. Once he has returned, economic factors and the clinical result in terms of continued gastric symptoms determine his further progress. Fortunately most patients achieve a diet upon which they can maintain weight, though they might not be able to gain on it.

The use of the intrajejunal tube was demonstrated to me by J. A. McDougal (1951, personal communication), who, like Stengel and Ravdin (1939), started the drip on return from the operating theatre. In the small series reported here there was some trouble in two cases with diarrhoea and distension, and subsequently the drip was started on the third morning and use made of the "polythene" tube already in place for gastric aspiration. Though the method is clearly effective for its purpose, it has disadvantages which restrict its use in clinical practice. The presence of a nasal tube, which in most post-operative routines is usual for the first two days, is probably not to blame for causing chest complications, but it certainly does help to perpetuate them and increase the difficulty of treatment. At least until post-operative chest complications are a less frequent occurrence, there will be many cases in which it seems undesirable to leave a nasal tube longer than is necessary for surgical safety. Nevertheless, in selected cases, particularly those patients who weigh 80% or less of standard before operation, the method deserves clinical consideration and further trial. It can be abandoned at any time if this seems desirable, and, while nothing is lost by trying the method, much may sometimes be gained by persisting with it.

Summary

Body weight before and after gastrectomy has been studied in 285 patients. Weight has been related to the standard weight for each individual.

At the time of operation 75% of patients were under standard weight. Those severely underweight (60–70% of standard) tended to do badly after operation, not only in terms of weight but by reason of continued gastro-intestinal complaints.

Loss of weight after operation occurred in 28% of patients. It is most pronounced in those patients who

previously were much over standard weight. Different patterns of post-operative weight loss are discussed.

Defective fat absorption follows gastrectomy, but the significance of this alone in relation to body weight is doubtful. Both dietary calorie intake and fat absorption are related to body weight, and failure to gain is greatest when both are impaired.

When loss of weight follows operation it occurs in the first few post-operative weeks, and thereafter the patient cannot regain it. The literature upon dietary requirements after severe weight loss and that dealing with the catabolic phase after injury or operation are reviewed.

Early post-operative drip feeding of a high-calorie high-protein mixture can prevent the loss of weight in the early post-operative period.

I wish to thank Mr. R. Marnham, who sponsored the work; the surgeons of St. George's Hospital for allowing me to investigate their patients; Professor Nicholas Martin for his advice and for affording me facilities in the Department of Biochemistry at St. George's; Professor T. Crawford and Dr. Hugh Gainsborough for much encouragement and help; and Dr. W. J. Martin for statistical advice. The weight tables were kindly lent by Dr. Malcolm Purvis.

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One of the subjects discussed at a recent meeting of the Fever Group of the Society of Medical Officers of Health at Fazakerley Hospital, Liverpool, was acute gastro-enteritis. Dr. E. BAILY (Park Hospital, London) summarized the bacteriological aspects, and drew attention to the importance of unmasking latent roughness in physically smooth colonies: the addition of a 1 in 500 solution of acriflavine to a saline suspension would at once cause auto-agglutination of serologically rough colonies and so prevent mistakes of interpretation. He showed slides illustrating finger contamination: a half-minute wash in antiseptic followed by a half-minute wash in running water was required for satisfactory cleansing. Dr. STANLEY BANKS (Park Hospital, London) dealt with the practical applications of bacteriological findings. Cubicles were no safeguard against cross-infection unless they were scrupulously clean: all unnecessary fittings must be removed, vacuum cleaning used, and small hand-towels, for use once only, provided. Nail brushes were often infected and were not necessary. Dr. R. B. MACKAY (Royal Children's Hospital, Manchester) and Dr. S. KEIDAN (University of Liverpool) gave brief reports on the use of polymixin and neomycin respectively in gastro-enteritis. Both antibiotics seemed to have an effect as least as good as other antibiotics on the disease: they appeared to have no toxic effects when given by mouth.

GAS TRANSPORT FUNCTION OF THE BLOOD IN CONGENITAL FAMILIAL METHAEMOGLOBINAEMIA

BY

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In normal blood only 1 to 2% of haemoglobin is present in the form of methaemoglobin, for, although methaemoglobin is constantly being formed by the oxidation of haemoglobin, there exists a very efficient mechanism within the red cell for the reduction of methaemoglobin to haemoglobin (Gibson, 1943). Methaemoglobin occurs clinically when drugs such as phenacetin or nitrites oxidize haemoglobin more rapidly than the normal reducing mechanism can function, or when there is an inherent defect in the reducing mechanism, as in congenital methaemoglobinaemia. Iron occurs in methaemoglobin in the oxidized or ferric form and the pigment is inert as an oxygen carrier.

It was first observed by Douglas *et al.* (1912) and by Barcroft *et al.* (1926) that the presence of abnormal derivatives of haemoglobin not only diminishes the oxygen capacity of the blood but also alters the readiness with which the blood releases oxygen to the tissues. The latter change is reflected in a shift of the oxygen dissociation curve. A shift of the curve to the left indicates an impaired release of oxygen to the tissues due to a greater affinity of haemoglobin for oxygen. Hitzenberger (1932) and Gibson and Harrison (1947) each found in one case of congenital methaemoglobinaemia a shift to the left of the oxygen dissociation curve. On the other hand, Litarczek *et al.* (1930), Eder *et al.* (1949), and Waisman *et al.* (1952) reported no alteration of the oxygen dissociation curve in single cases of methaemoglobinaemia.

In view of the conflicting nature of these reports the opportunity was taken to study gas transport in two cases of familial methaemoglobinaemia.

Case 1

A married woman aged 44 was admitted to hospital in March, 1953, for an operation for hallux valgus and vari-

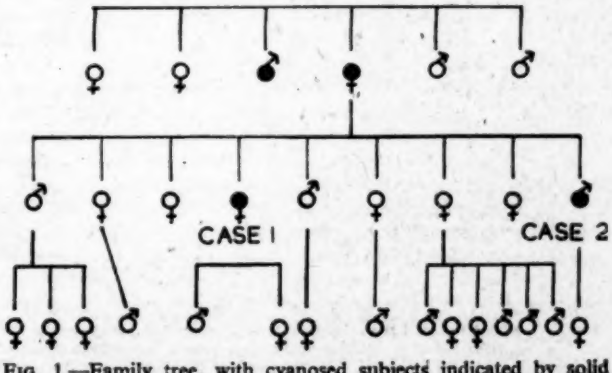

FIG. 1.—Family tree, with cyanosed subjects indicated by solid symbols, Case 1 and 2 having proved methaemoglobinaemia.

cose veins. She was cyanosed, and she said that she had been so throughout her life. There was a family history of cyanosis (Fig. 1) but some years previously, when in a maternity hospital, she had been told she had congenital heart disease. The cyanosis varied from day to day, was worse in winter, and was never entirely absent. There was no history of dyspnoea or undue fatigue.

On examination the patient was pale and cyanosed. The cyanosis had no special quality to distinguish it from the cyanosis of cardiac or respiratory disease, although it was more intense than the usual cyanosis due to cardiac or respiratory disease. There was no clubbing of fingers. Apart from the cyanosis and the disabilities for which she sought surgical treatment, clinical examination was negative. The patient's two children (Fig. 1), aged 18 and 17, were examined, and neither was found to be cyanosed, nor was methaemoglobin detected.

Methaemoglobin was identified spectroscopically in the patient's venous blood, and the results of estimations before and during treatment with ascorbic acid and methylene blue, together with other laboratory findings, are shown in the Table and Figs. 2, 3, and 4.

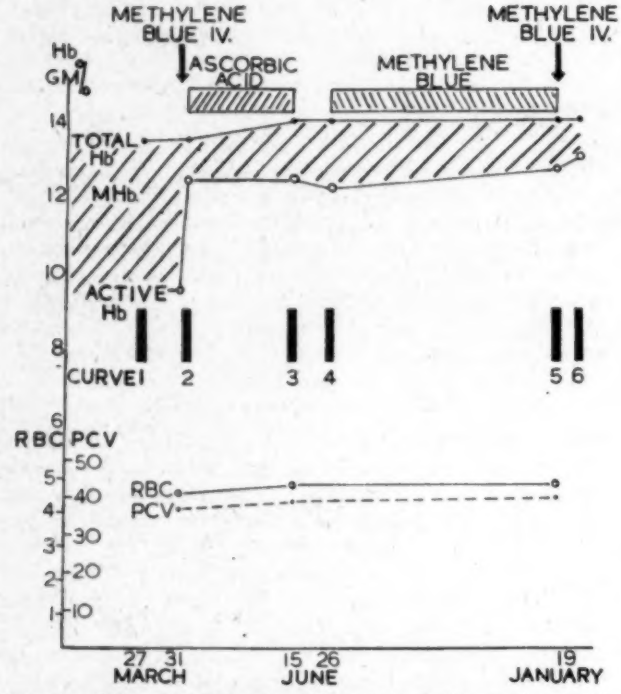

FIG. 2.—Effect of treatment with methylene blue and ascorbic acid on methaemoglobin levels in Case 1. The times of oxygen dissociation curve studies are indicated.

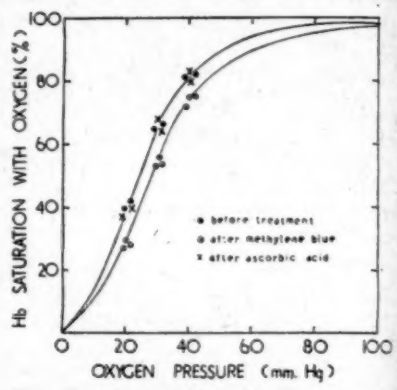

FIG. 3.—Oxygen dissociation curve in Case 1 before treatment and after ascorbic acid (shifted to the left), and after treatment with methylene blue (normal).

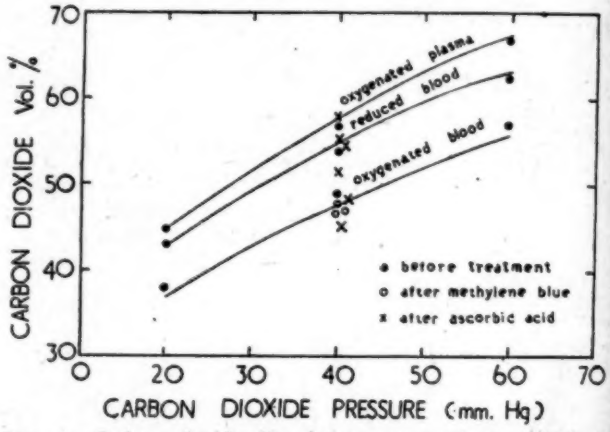

FIG. 4.—Carbon dioxide dissociation curves of normal blood compared with values determined for Case 1.

Results of Laboratory Findings

Curve No.	Date	Time	R.B.C. Mill./c.mm.	P.C.V. %	Total Pigment G.%	O_2 Carrying Hb		Met Hb		Pressure CO_2 mm. Hg	(Total CO_2)$_o$* Vol. %	(Total CO_2)$_r$† Vol. %	(Total CO_2)$_b$ Vol. %	pH_a‡	PO_2 for Hb=HbO_2§		HbO_2 Vol. % at PO_2=20	I/K
						HbO_2 Vol. %	G.%	G.%	Total Pigment %						pH_a	pH_a=7.4		
Case 1																		
1	27/3/53	Before treatment	4·5	37	13·5	13	9·5	4	30	20	38	43	45	7·61			55	1,500
										40	49	54	56	7·39	23	22·5	40	2,700
										60	57	63	67·5	7·29			32	3,700
2	31/3/53	After methylene blue i.v.	4·5	37	13·5	17	12·5	1	6	40	48	55	57·5	7·40	26·5	26·5	33	3,500
3	15/6/53	After ascorbic acid orally				16·5	12·5	1·5	10	40	48	55	57	7·40	23	23	40	2,700
4	26/6/53	"	4·8	39	14	16	12·2	1·8	12	40	45	52	55	7·38	23	22	40	2,600
5	19/1/54	After methylene blue orally	4·8	40	14	17	12·7	1·3	9	40	47		56	7·39	27·5	27	32	3,800
6	19/1/54	After methylene blue i.v.				17·5	13	1	6	40	46		55·5	7·38	27	26	33	3,500
Case 2																		
1	22/9/53	Before treatment		52	18	19	13·5	4·5	25	20	34	40	43	7·58			54	1,600
										40	45	52	55	7·38	23·5	23	39	2,900
										60	52	60	65	7·27			32	3,700
Mean values for normal blood						19·5			2	20	37	43	44	7·60			46	2,100
										40	48	55	57	7·40	27	27	33	3,600
										60	56	64	69	7·30			26	5,200

* (Total CO_2)$_o$=Total carbon dioxide of oxygenated blood at a CO_2 partial pressure of 40 mm. Hg.
† (Total CO_2)$_r$=Total carbon dioxide of reduced blood at CO_2 partial pressure of 40 mm. Hg.
‡ pH_a=Plasma pH determined in true plasma from blood saturated with oxygen when PCO_2 equals 40 mm. Hg.
§ PO_2 for Hb=HbO_2=Partial pressure of oxygen at which haemoglobin saturation with oxygen is 50% at the plasma pH of the recipient and at standard plasma pH of 7·4.
K=Affinity constant of haemoglobin for oxygen.

Case 2

This patient, a man aged 32, is the only sibling (Fig. 1) of Case 1 with a history of cyanosis. Cyanosis was clinically more striking than in Case 1, but pallor was not present. There was no history of dyspnoea, fatigue, or headache or any evidence of cardiac or respiratory disease. As in Case 1, methaemoglobin was identified spectroscopically in the patient's blood: the results of laboratory findings are shown in the Table.

Methods

Methaemoglobin was identified by the presence of an absorption band at 630 mμ which disappeared on the addition of a few drops of 10% sodium cyanide. For this examination a Hartridge reversion spectroscope was used. Methaemoglobin was estimated by a modification of the method of Evelyn and Malloy (1938), using an S.P. 600 spectrophotometer, and by gas analysis (Peters and Van Slyke, 1931). Total haemoglobin was estimated after conversion to cyanmethaemoglobin as described by Evelyn and Malloy (1938). It is worthy of note that even when methaemoglobin accounted for 20–30% of the total haemoglobin the characteristic absorption band could not easily be seen in a 10% aqueous dilution of blood in a 1-cm. layer, using the reversion spectroscope.

Oxygen and carbon dioxide dissociation curves were obtained as described by Valtis and Kennedy (1954). The value I/K at different *p*H was determined from the Hill–Barcroft equation, taking n=2.5 (Adair, 1925), by equilibrating blood in tonometers at a standard oxygen pressure of 20 mm. Hg and at various CO_2 pressures (20, 40, and 60 mm. Hg). All the values for CO_2 in the serum of whole blood, whether reduced or oxygenated, were directly determined because of the unknown properties of methaemoglobin in this physico-chemical system.

Results

In both cases, before treatment, when methaemoglobin levels were 30% and 25% respectively, the oxygen dissociation curves showed a shift to the left. In Case 1 this was corrected after treatment with methylene blue, when, on three occasions with methaemoglobin values of 6, 9, and 6%, the oxygen dissociation curve was found to be normal. After treatment with ascorbic acid, with methaemoglobin values of 10 and 12%, the oxygen dissociation curve on two occasions was abnormal. These and other results are set forth in detail in the Table and in Figs. 2, 3, and 4. Conventional symbols, the meanings of which are explained in the footnotes to the Table, are used for the headings of several of the columns. The position of the oxygen dissociation curve is indicated by the partial pressure of oxygen at which 50% of the haemoglobin is oxygenated and by the affinity constant K.

In both cases the oxygen dissociation curve before treatment was shifted to the left both at the *p*H of the blood and at standard *p*H (see Table). The value of I/K was found to be 2,700, compared with mean values of 3,600 in six normal subjects. The values of I/K plotted against the partial pressure of CO_2 are in these cases of methaemoglobinaemia proportional to but much smaller than the normal.

When considering results for carbon dioxide due allowance must be made for the amount of total pigment present in reduced blood and for active haemoglobin in oxygenated blood. When this was done the position and slope of the carbon dioxide dissociation curves, the difference in the CO_2 content of reduced and oxygenated blood, and the difference between CO_2 content of true oxygenated plasma and oxygenated whole blood were all within normal limits.

In Case 1, after treatment with methylene blue intravenously, the oxygen dissociation curve and consequently the relationship of I/K to the partial pressure of CO_2 both became normal. The position of the CO_2 dissociation curve of reduced and oxygenated blood, and the CO_2 difference between them, also became normal. Later, after treatment with ascorbic acid, the oxygen dissociation curve on two occasions was found to have the same abnormality as before treatment. The carbon dioxide dissociation curves for reduced and oxygenated blood were normal. Still later, after prolonged treatment with methylene blue, the oxygen dissociation curve was once more normal in shape and position.

Discussion

As has already been mentioned, Hitzenberger (1932) found in a case of congenital methaemoglobinaemia a shift to the left of the oxygen dissociation curve. Gibson and Harrison (1947) also found a similar alteration in a single case of familial congenital methaemoglobinaemia. At an earlier date Litarczek *et al.* (1930) observed a slight shift of the oxygen dissociation curve to the left in a case of congenital methaemoglobinaemia, but it was attributed by these workers to an alteration in the alkalinity, buffering capacity, and the I/K to *p*H relationship of the patient's blood, rather than to the presence of methaemoglobin *per se*. Eder *et al.* (1949) reported an investigation at the Harvard Fatigue Laboratory of a case of congenital methaemoglobinaemia in which the oxygen dissociation curve was found to be normal in position; and Waisman *et al.* (1952) described a similar finding in another case.

In our two siblings with familial congenital methaemoglobinaemia with 25 to 30% methaemoglobin we found the oxygen dissociation curves to be shifted to the left, both at the actual *p*H of the blood and when corrected to standard *p*H. This shift was less in magnitude than that described by Hitzenberger (1932) in his patient with methaemoglobinaemia, but was substantially the same as that reported by Gibson and Harrison (1947). When allowance was made for the inactive pigment present, the position and slope of the carbon dioxide dissociation curves were found to be normal. When considered in relation to the Hill–Barcroft equation

$$vCO_2 = c + b\,(cH \times 10^6)$$

this finding removes any suspicion that the alkalinity (value c) or the buffering capacity (value b) of the blood might be responsible for the altered oxygen dissociation curves. Similarly, changes in the value I/K plotted against the partial pressure of carbon dioxide, which indicates the relationship between the affinities of haemoglobin for oxygen at different *p*H, were proportional to changes occurring in normal blood.

Darling and Roughton (1942) reported observations on the oxygen dissociation curve of blood containing methaemoglobin prepared by the oxidation of haemoglobin *in vivo* and *in vitro*. By using solutions of laked blood in strong phosphate buffer they avoided interference by corpuscular factors and by *p*H changes due to varying degrees of haemoglobin saturation with oxygen. In addition, they studied the oxygen dissociation curve without adding carbon dioxide to the tonometers and were thus able to exclude its effect. They found a shift to the left of the oxygen dissociation curve proportional to the amount of methaemoglobin present and concluded that these findings were attributable to the presence of molecules of both haemoglobin and methaemoglobin containing the ferrous and ferric atoms in various atomic proportions.

Since methaemoglobin in sufficient concentration is itself thought to be responsible for the shift of the oxygen dissociation curve, it was natural in our case to expect this abnormality to be abolished by effective treatment. Three curves were performed after treatment with methylene blue, and all were found to have returned to normal. Gibson and Harrison (1947) have reported a similar return to normal after the addition of methylene blue to the blood of their patient *in vitro*. During and after treatment with ascorbic acid the oxygen dissociation curve was

studied on two occasions, and both curves showed a shift to the left of the same magnitude as before treatment.

The seeming contradiction between our findings on the one hand and those of Eder *et al.* (1949) and Waisman *et al.* (1952) on the other may be resolved by postulating the existence of two or more kinds of congenital methaemoglobinaemia not completely distinguished by methods at present available. On very different grounds Lutembacher (1947) and Hörlein and Weber (1948) have made similar suggestions. An alternative explanation is that it is not methaemoglobin itself but some other factor which is responsible in congenital methaemoglobinaemia for the abnormality of the oxygen dissociation curve. From our findings it would seem that this factor must be influenced differently by ascorbic acid and by methylene blue. It was found by Litarczek *et al.* (1931) that glutathione exerts an influence on the oxygen dissociation curve, and it seems to us that glutathione has been inadequately investigated in methaemoglobinaemia.

The mode of inheritance of familial methaemoglobinaemia is still uncertain. A family tree suggestive of a Mendelian dominant character has been reported by Baltzan and Sugarman (1950). On the other hand, Gibson and Harrison (1947) and Codounis (1952) each described a family in which inheritance as a recessive character seems more likely. In our family, too (Fig. 1), inheritance as a recessive character seems the more probable.

Summary

The oxygen dissociation curves of two cases of familial congenital methaemoglobinaemia have been studied.

A shift of the curve to the left was found in both cases. This indicates impaired efficiency of oxygen delivery to the tissues in addition to what is attributable to loss of oxygen capacity due to the presence of an inert pigment.

Treatment with methylene blue restored the curve to normal. After treatment with ascorbic acid the curve remained abnormal.

These observations and published reports of similar studies are discussed. It is concluded either that there is more than one kind of congenital methaemoglobinaemia or that the alteration in oxygen transport in the condition is due to some factor other than methaemoglobin itself.

We are grateful to Professor L. J. Davis for his advice and criticism in the preparation of this paper; to Dr. J. H. Wright and the late Mr. A. M. Clark, who gave us the opportunity to study Case 1; and to Dr. H. J. R. Kirkpatrick and Dr. D. W. D. MacLaren, whose help enabled us to study Case 2. One of us (D. J. V.) was enabled to undertake this work by scholarships from the E.C.A. for Greece and from the University of Thessaloniki. The expenses of the investigation were met in part by a grant from the Board of Management of Glasgow Royal Infirmary and in part by the Rankin Fund of the University of Glasgow.

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BLOOD CHANGES ASSOCIATED WITH DISSEMINATED TUBERCULOSIS

REPORT OF FOUR FATAL CASES AND REVIEW

BY

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Although anaemia is common to all forms of tuberculosis it is rarely severe (Wintrobe, 1951), and usually normochromic or hypochromic. Chapman and Whorton (1946), in a clinico-pathological study of 63 cases of generalized miliary tuberculosis, noted a moderate normochromic anaemia in 84%. The lowest haemoglobin level was found to be 43%, the level in the majority ranging from 65% to 85%. The white-cell count was persistently low for two weeks or more in 11 out of a total of 49 patients in the above series, a relative neutrophilia being usually associated with leucopenia. The haematological picture in two cases resembled aplastic anaemia, and the presence of immature white cells and nucleated red cells in one case suggested a leuco-erythroblastic anaemia. Dyke (1924) recorded a case with generalized miliary tuberculosis associated with aplastic anaemia. Rosenthal (1928) has reported on aplastic anaemia as a complication of miliary tuberculosis, and referred to the haemorrhagic diathesis sometimes resulting from thrombocytopenia. Crail *et al.* (1948) described four cases of miliary tuberculosis associated with myelofibrosis and suggested that tuberculosis was the predisposing factor in the marrow changes. The same authors stated that the bone marrow in miliary tuberculosis shows, in the early stages, hyperplasia of all haemopoietic tissue, followed later by hypoplasia or aplasia.

Bone-marrow infiltration by disease in miliary tuberculosis seems to be not uncommon, Chapman and Whorton (1946) describing its presence in 33 out of 37 cases at necropsy. They believed that the presence of miliary tubercles in bone marrow did not necessarily predispose to depression of blood formation. Doan and Sabin (1927) produced extensive tuberculous lesions of the bone marrow of rabbits following the intravenous injection of virulent tubercle bacilli. There was an initial depression of marrow function, as judged by peripheral blood studies, followed, in animals that survived, by compensatory hyperactivity and finally by functional and morphological recovery.

In the rare condition of tuberculous splenomegaly, cytopenic states are recognized as being due to a hypersplenic mechanism, the bone marrow being normal or hyperplastic (Engelbreth-Holm, 1938). Polycythaemia has also been recorded in association with tuberculous splenomegaly (Guild and Robson, 1950).

Leukaemoid reactions accompanied by leucocytosis and the presence of immature white cells in the peripheral blood, making a differentiation from myeloid leukaemia difficult, is mentioned by Forkner (1938). Gardner and Mettier (1949) described a lymphocytic leukaemoid reaction of the blood associated with miliary tuberculosis.

Muller (1943) reviewed in detail the clinical significance of the blood changes associated with tuberculous infection.

The following four cases of generalized tuberculosis are reported in view of the profound haematological

changes which accompanied the disease, and because of the problems entailed in diagnosis.

Case 1

A housewife aged 22 was admitted to the Leeds General Infirmary on November 11, 1949. Her main complaints were increasing weakness, nervousness, sweating, and loss of weight for one year. Her past history and family history were negative. On examination she was extremely pale. Her skin was hot and moist, temperature 102.5° F. (39.2° C.). She was very nervous, with a tremor of the outstretched hands, and she had lost weight. There was no thyroid enlargement or exophthalmos, and, apart from tachycardia, no other abnormalities were discovered on clinical examination.

Investigations.—*X*-ray examination of the chest showed no evidence of lung disease. A blood examination gave the following results: Hb, 46% (Haldane); red cells, 1,900,000 per c.mm.; C.I., 1.21; M.C.V., 105 μ^3; reticulocytes, 5%; white cells, 4,000 (neutrophils 51%, lymphocytes 49%); platelets, 125,000; bleeding time, 2 minutes; E.S.R. (Westergren), 50 mm. in first hour. A blood film showed the red cells to be well haemoglobinized, and macrocytosis was prominent. A relative lymphocytosis was noted, but immature cells were not seen. A sternal bone-marrow examination revealed a severe depression of red- and white-cell-forming tissue, erythropoiesis being normoblastic. The differential marrow count showed 87% lymphocytes. A Rehfuss test meal showed a histamine-fast achlorhydria. The erythrocyte fragility was normal and urine urobilinogen was absent. Further tests were reported as follows: cephalin-flocculation test, negative; gold-sol, No. 2; thymol turbidity, 7.3 units; plasma proteins, total 6.8 g. per 100 ml.; A./G. ratio, 1 : 6; alkaline phosphatase, 6 units; blood urea nitrogen, 13.3 mg. per 100 ml.; blood calcium, 10.9 mg. per 100 ml.; phosphorus, 4.1 mg. per 100 ml. *X*-ray examination of the skeleton revealed nothing abnormal. Blood culture and agglutination tests for typhoid, paratyphoid, dysentery, and *Br. abortus* were negative.

The blood picture which further examination revealed was that of a leuco-erythroblastic anaemia with evidence of severe depression of bone-marrow function. The diagnosis was obscure, and atypical Hodgkin's disease, or lymphosarcoma, and aleukaemic leukaemia were regarded as possibilities.

In view of the continuous swinging temperature treatment with penicillin was instituted. No satisfactory response was obtained. The patient was given blood transfusions and discharged home at her own request on December 11.

She was readmitted on March 16, 1950, complaining of excessive fatigability, a throbbing pain in the head, night sweats, frequency of micturition, and polydipsia. On examination she was severely anaemic; temperature, 103.4° F. (39.7° C.). Systemic examination was otherwise negative. Blood examination showed: Hb, 38%; red cells, 1,500,000; C.I., 1.26; white cells, 1,200 (polymorphs, 25%, lymphocytes 75%); platelets, 80,000. A blood film showed macrocytosis, myelocytes, and erythroblasts. The sternal marrow revealed no change, the differential cell count showing 80% lymphocytes. *X*-ray examination of the chest revealed normal findings. Antibiotics and blood transfusions were again prescribed, but little change in her condition resulted. The spleen became palpable just before her discharge home in May, 1950.

She was again admitted to hospital in July, 1950, when extreme cachexia, anaemia, high fever, and splenomegaly were found to be present. In view of the development of a toxic psychosis she was transferred to a psychiatric ward at St. James's Hospital, Leeds, where she developed a terminal pericarditis and died on August 7, 1950.

Post-mortem examination showed evidence of miliary tuberculosis affecting the abdominal lymph nodes, the liver, spleen, and pericardium. The lungs, kidneys, brain, and pelvic organs were normal. The bone marrow was unfortunately not examined. There was no evidence of extramedullary haematopoiesis in the sections of the liver, spleen, or lymph nodes examined.

Case 2

A female brass-feeder aged 51 was admitted to St. James's Hospital, Leeds, on March 11, 1950, with a four-months history of increasing weakness, lassitude, and dyspnoea on exertion. For a similar period her appetite had deteriorated and she had complained of recurrent attacks of central abdominal pain, associated with nausea and vomiting. She had lost 3 stone (19 kg.) in weight. There was no history of previous illness or any relevant family history.

Examination showed her to be of low intelligence and uncooperative. The temperature was 101.4° F. (38.6° C.), and she was moderately anaemic. The lower pole of the spleen was 3 in. (7.5 cm.) below the left costal margin. No other abnormality was noted.

Investigations.—*X*-ray examination of the chest, stomach, and duodenum showed no abnormality. No occult blood was detected in the faeces. A Rehfuss test meal revealed a histamine-fast achlorhydria. The urine contained a trace of albumin, and hyaline and granular casts were seen on microscopical examination. Blood examination showed: Hb, 60% (Haldane); red cells, 2,500,000; C.I., 1.2; M.C.V., 109 μ^3; reticulocytes, 5.4%; white cells, 2,600 (neutrophils 81%, eosinophils 3%, basophils 1%, lymphocytes 8%, monocytes 7%); platelets, 37,000. A blood film showed fully haemoglobinized red cells, macrocytosis, and anisocytosis. Platelets were scanty. E.S.R. (Westergren) 60 mm. in first hour. The sternal bone marrow was markedly hypocellular. Apart from the reduction in absolute numbers, the differential marrow cell count showed a preponderance of lymphocytes. The predominant cell in the erythroid series was the normoblast, and few early forms were seen. No megaloblasts were identified. Erythrocyte fragility was normal, lysis beginning at 0.44% of saline and complete at 0.32% of saline. Schumm's test was negative. Urobilinogen was not present in the urine, and the faecal urobilinogen was normal at 117.1 mg. per 100 g. The serum bilirubin was 0.8 mg. per 100 ml.; plasma proteins, 6.8 g. per 100 ml., A./G. ratio, 1:6; thymol turbidity, 4 units. An intravenous pyelogram demonstrated a normal renal tract and the blood urea nitrogen was 15 mg. per 100 ml.

At this stage the essential findings were persistent pyrexia, splenomegaly, and pancytopenia associated with a severe depression of all blood-forming elements in the bone marrow. There was no evidence of the nature of the underlying disease.

On April 1 a painful lymph-node enlargement which was hard and tender developed on the left side of the neck. There was no sore throat or obvious focus of infection. The symptoms abated within the next two days, but as the enlarged gland persisted it was removed on April 23. Histological examination showed caseation and epithelioid reaction characteristic of tuberculosis. Scanty tubercle bacilli were demonstrated in the section. Further chest radiographs revealed nothing abnormal and tubercle bacilli were not isolated from the sputum.

The abdominal pain and vomiting cleared shortly after admission to hospital, but otherwise her condition remained unchanged. The pyrexia was not controlled by penicillin, and blood transfusions were given in an attempt to improve the blood picture and the patient's general condition. Repeated blood examinations, however, continued to show the presence of anaemia, macrocytosis, leucopenia, thrombocytopenia, and reticulocytosis. No further clinical evidence of tuberculosis appeared.

On May 12 the patient was transferred to a convalescent home, but owing to her rapid deterioration she was readmitted to hospital 11 days later. She was pyrexial and cachectic; splenomegaly was pronounced; B.P. 115/75. Systemic examination revealed nothing abnormal. Blood examination: Hb, 58%; red cells, 3,000,000; reticulocytes, 4.3%; white cells, 3,100 (polymorphs 78%, lymphocytes 9%,

myelocytes 6%, metamyelocytes 4%, monocytes 3%); platelets, 50,000. Nucleated red cells were present in a blood film.

On May 27 she became restless, and early the next day was semicomatose. The blood urea nitrogen was raised to 68 mg. per 100 ml. and death occurred 24 hours later.

Post-mortem examination showed evidence of miliary tuberculosis involving the liver, spleen, kidneys, adrenal glands and bone marrow. The primary focus was present in a Fallopian tube. No evidence of extramedullary haematopoeisis was observed in the spleen, liver, or lymph nodes.

Case 3

A motor driver was admitted to the Leeds General Infirmary on October 22, 1948. His medical history began in April, 1948, when he developed a severe frontal headache which persisted for about 10 days and was followed by an erythematous eruption which first appeared along the hair margin of the forehead and spread to involve the right eyebrow, the pinnae, and the shoulder regions. Pustular formation followed. The eruption gradually disappeared, but about a month later he developed a severe pain in the right knee and ankles, associated with pyrexia and profuse sweating. There was no swelling of the joints, and salicylates afforded only very slight and temporary relief. He also developed a dry cough, a tightness in the chest, constipation, and marked weakness. During the next eight weeks he was confined to bed and lost 35 lb. (15.9 kg.) in weight.

In June he was admitted to the County Hospital, Driffield, as a suspected case of tuberculosis. On examination at that time he was noted to have lost weight and to be severely anaemic. His temperature was 101.4° F. (38.6° C.), B.P. 120/90. Systemic examination gave no abnormal findings. Various investigations, including *x*-ray examination of the chest and gastro-intestinal and renal tracts, blood culture, agglutination tests, plasma chlorides, and proteins, showed normal findings. Liver-function tests, however, suggested some impairment of function. Blood examination revealed a pronounced pancytopenia and macrocytosis, but no immature cells were observed on examination of a blood film. The sternal bone marrow was of normal cellularity and had a normal myeloid–erythroid ratio. Treatment with penicillin, liver extract, and folic acid failed to have any effect on the temperature or blood picture, and the patient was transferred to the Leeds General Infirmary for further investigation.

On examination on October 22 he was cachectic, pyrexial, and anaemic. The liver was palpable three fingerbreadths below the right costal margin. There was no splenomegaly. Examination of other systems revealed no abnormalities.

Investigations.—Blood examination showed: Hb, 54%; red cells, 2,600,000; C.I., 1.04; P.C.V., 26%; M.C.V., 100 μ^3; M.C.H.C., 30%; white cells, 1,300 (neutrophils 65%, eosinophils 1%, lymphocytes 32%, monocytes 2%); platelets, 90,000; E.S.R., 41 mm. in first hour. The blood film showed macrocytosis and one nucleated red cell per 100 white cells; clotting-time, 4 minutes; prothrombin time, 19 seconds. Bone marrow was of normal cellularity with a normal differential count. Sternal biopsy showed normal bone marrow. Agglutination tests for typhoid, paratyphoid A and B, and *Br. abortus* were negative. The plasma proteins totalled 6 g. per 100 ml. (albumin 1.9 g., globulin 4.1 g., per 100 ml.; A/G ratio 0.46); thymol turbidity, No. 8; gold-sol, No. 5; blood cholesterol, 100 mg. per 100 ml. Blood culture was negative. Repeated sputum examinations for tubercle bacilli were negative.

The patient's condition remained stationary during the first week and then rapidly progressed downhill, with high fever, sweating, tachycardia, and exhaustion. Penicillin failed to control the fever, and in view of the past history of dysentery while on active service in India and the enlarged liver a course of emetine hydrochloride was prescribed although no diagnostic proof of amoebiasis had been obtained. No response to treatment occurred. Right-sided pleural effusion was confirmed by an *x*-ray film of the chest, which also revealed a patchy increase in density of a nodular type throughout both lung fields. The report stated that "the appearances are not typical of miliary tuberculosis, but such a lesion cannot be excluded." Further attempts to isolate tubercle bacilli were unsuccessful, and the patient died two weeks after admission to the infirmary with the diagnosis still in doubt.

Post-mortem examination showed massive caseating tuberculous lesions affecting both lungs. Widespread crude tubercles from 1 to 10 mm. in diameter were found in the lungs, liver, spleen, and kidneys. There were submiliary tubercles in the adrenal glands, a gross tuberculous lesion of the prostate, and localized tuberculous peritonitis with adhesions over the liver and spleen. Extensive pleural adhesions were noted on the right side, and effusions were present at both bases.

Case 4

A housewife aged 61 was admitted to the Leeds General Infirmary on November 1, 1951. Her symptoms began after an attack of tonsillitis 10 months previously, when she complained of increasing lassitude, weakness, anorexia, and slight loss of weight. During the six months before admission she had become much paler and complained of severe palpitations and breathlessness on exertion. No obvious bleeding had been noticed, but for two weeks she had been troubled with a burning epigastric discomfort following meals which was inconstant and never severe. She had had no previous serious illnesses and the family history was one of good health.

On examination she was seen to be extremely anaemic and dyspnoeic on the least exertion. The cervical lymph nodes on the left side were enlarged and a solitary enlarged left axillary node was palpable. Haemorrhages were present in the fundus oculi on both sides. The skin over the abdomen was dry and loose and the tip of the spleen was palpable. There was no hepatomegaly. Examination of other systems revealed no abnormality. The temperature was 100.4° F. (38° C.), pulse 92, and B.P. 140/70.

Investigations.—Blood examination showed: Hb, 32%; red cells, 1,300,000; C.I., 1.23; white cells, 4,000 (polymorphs 28%, bands 3%, lymphocytes 64%, monocytes 4%, eosinophils 1%); platelets, 110,000. The blood film revealed macrocytosis, anisocytosis, and poikilocytosis. The bleeding-time was 3½ minutes, and the clotting-time 4½ minutes. The sternal bone marrow showed 98% lymphocytes, many of them immature. A Rehfuss test meal demonstrated a hyperchlorhydria and *x*-ray examination of the chest was normal.

In view of the haematological findings, together with the enlarged lymph nodes and splenomegaly, the probable diagnosis was thought to be aleukaemic lymphatic leukaemia. Blood transfusions corrected the anaemia. The patient was discharged home on November 28.

She was readmitted on January 7, 1952, in view of progressive pallor, weakness, and dyspnoea. Examination showed considerable weight loss, severe anaemia, and widespread purpura. The enlarged lymph nodes in the neck were more prominent and the spleen was palpable. There was no hepatomegaly. Blood examination revealed a pancytopenia, the Hb being 52%; white cells, 4,000 (polymorphs 45%, lymphocytes 45%, bands 10%); platelets, 70,000. A further bone-marrow examination was not performed. Blood transfusions were again given, but a rapid downhill course followed, and the patient died on January 26.

Post-mortem examination revealed widespread caseating tuberculosis involving the cervical and axillary lymph nodes, the lungs, spleen, and liver. In addition considerable infiltration of these organs by lymphoid cells was observed, indicating a coexisting lymphatic leukaemia.

Comment

The four cases described above presented with profound haematological abnormalities. A pancytopenia was present in all from the outset. Anaemia was severe; in three

patients the haemoglobin was below 50%, the lowest reading being 32%. Macrocytosis was present in all, and the bone marrow showed marked depression of haematopoiesis in three cases.

In Cases 1 and 2 the bone-marrow picture suggested aplastic anaemia, although, as is not unusual, aleukaemic lymphatic leukaemia was difficult to eliminate by marrow aspiration alone. Persistent reticulocytosis and a leuco-erythroblastic anaemia in the absence of myeloid metaplasia indicated that some marrow function remained. A possible explanation for the leuco-erythroblastic anaemia may have been infiltration of the bone marrow by the tuberculous process. Chapman and Whorton's series, however, indicated that a leuco-erythroblastic picture was rare, while miliary spread to the bone marrow was a common finding. In Case 3 the bone marrow was normal, and the absence of splenomegaly contraindicated a hypersplenic mechanism as the cause of the cytopenia. Case 4 was remarkable in that, although clinically showing many haematological features similar to those of the other cases, post-mortem examination showed that it differed in that widespread visceral infiltration with lymphoid cells was present, indicative of a co-existing lymphatic leukaemia. Although lymphatic leukaemoid reactions have been reported (Gardner and Mettier, 1949) to be associated with miliary tuberculosis, the presence together of leukaemia and generalized tuberculosis must be extremely rare. Forkner (1938) has reviewed this subject. Of much interest was the fact that the patient's previous history was one of good health and there was no suggestion of previous tuberculosis. A possible explanation for the dual findings may have been the presence of a latent focus of tuberculosis which was exacerbated by the developing leukaemia, with resulting widespread dissemination.

From the clinical standpoint the cases presented were primarily problems in diagnosis, of which the cardinal feature was the presence of marked haematological changes, together with pyrexia and progressive weight loss. In only one instance was a definite diagnosis reached before death (Case 2), following the appearance and biopsy of an enlarged lymph node in the neck. Case 1 showed no clinical evidence of tuberculosis at any time during the course of the disease, while routine investigations for tuberculosis in Case 3 were negative, although latterly the *x*-ray findings of the chest were suggestive. A clinical diagnosis of aleukaemic lymphatic leukaemia was made in Case 4, and it was not until necropsy that the enlarged lymph nodes and spleen, in life considered to be due solely to leukaemic infiltration, were found also to be the seat of extensive tuberculous disease.

In view of the present chemotherapeutic agents available for the treatment of tuberculosis it is essential that an early diagnosis be made. As in the above cases, in the presence of pancytopenia with or without depression of the blood-forming elements in the bone marrow, together with pyrexia and loss in weight, and in the absence of any other causative factor, tuberculosis should be considered. The presence of lymphadenopathy demands a biopsy in order to differentiate from Hodgkin's disease, or lymphosarcoma, and aleukaemic lymphatic leukaemia. In addition to routine diagnostic procedures, the bone marrow should be examined for the presence of miliary tubercles either following trephine biopsy or by the technique described by Schleicher (1946). Culture of blood obtained by bone-marrow aspiration, together with guinea-pig inoculation, should also be carried out in an attempt to demonstrate the presence of tuberculous disease.

Summary

Four cases of disseminated tuberculosis are described associated with pancytopenia and macrocytosis. The bone marrow in one was normal, but in three cases a profound depression of the blood-forming elements in the bone marrow, with a preponderance of lymphocytes, was present. In two a leuco-erythroblastic anaemia was observed, and aleukaemic lymphatic leukaemia together with generalized tuberculous disease was observed at necropsy in one instance.

The difficulties entailed in diagnosis are described and suggestions made regarding the procedure likely to prove helpful in similar cases.

I wish to thank Professor R. E. Tunbridge and Dr. S. J. Hartfall for permission to publish details of cases under their care.

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CARDIAC ARREST UNDER ANAESTHESIA DURING INDUCTION OF LABOUR WITH "PITOCIN" DRIP

BY

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The intravenous use of the oxytocic principle of the pituitary seems now to be established practice in obstetrics, and successful results are causing it to be more widely used. A recent fatality, which appeared to result directly from the administration of a continuous intravenous "pitocin" (oxytocin) drip, is recorded to draw attention to the fact that there are circumstances in which the practice is not free from danger.

Case Report

A 4-para aged 41, who was two weeks past her expected date of delivery, was admitted to hospital because of painless vaginal bleeding. The blood loss was estimated at about half a pint (285 ml.).

There was no abnormality of the heart or lungs, the blood pressure was 130/60, and the urine was free from albumin. The vertex was presenting and the head was high. A provisional diagnosis of placenta praevia was made, and it was thought advisable to examine her under anaesthesia, with full preparation to proceed to caesarean section if this should seem necessary. Blood was cross-matched for the patient. She was given an injection of atropine, 0.65 mg., one hour before the time fixed for operation.

Because the preliminary examination would necessarily delay the delivery of the foetus should caesarean section be undertaken it was thought best to avoid thiopentone altogether and to use only cyclopropane and oxygen in a closed circuit. Induction was smooth and uneventful, and within five minutes it was possible for the obstetrician to begin his examination. At the same time an intravenous drip of 5% glucose-saline was set up.

Examination showed the cervix to be two fingerbreadths dilated, with the membranes bulging through. On further examination to feel the position of the placenta the membranes were ruptured accidentally. The lower edge of the separated placenta was felt about 1 in. (2.5 cm.) above the edge of the cervix, situated anteriorly. This examination provoked brisk bleeding, which was quickly controlled by fundal pressure and pushing the head of the foetus into the pelvic brim. In view of the fact that the bleeding was controlled in this way it was decided that caesarean section was unnecessary, as labour could be induced immediately by the use of a pitocin drip. Since we were aware of possible danger from the combination of "pituitrin" and cyclopropane the administration was delayed while the anaesthetist washed away the cyclopropane with a rapid flow of nitrous oxide and oxygen, the haemorrhage being meanwhile controlled by fundal pressure.

After five minutes the face-mask was removed, the patient showed signs of returning consciousness, and word was given for the addition of 30 units of pitocin to the fluid remaining in the 1,000-ml. saline bottle. Within a minute or two of the start of the flow of the pitocin the patient became cyanosed; the intravenous drip was immediately stopped, and the lungs were inflated with oxygen, but without improvement, and it was evident that the heart had stopped though respiration was still present. An injection of 10 ml. of 1% procaine was immediately given into the left ventricle, followed by 0.5 ml. of adrenaline, while the surgeon opened the abdomen and diaphragm to massage the heart. Strenuous efforts at resuscitation were continued for 75 minutes before being finally abandoned.

One point of interest is that, although the characteristic wormlike contractions of ventricular fibrillation were felt, some spontaneous cardiac contractions did later occur in response to massage; these were, however, weak and ineffective and were not long maintained. An attempt was made to estimate from the fluid level in the saline bottle how much pitocin had actually reached the patient, but uncertainty regarding the exact level of the saline at the time of adding the pitocin made calculation impossible.

Post-mortem examination confirmed the obstetrical findings, and showed in addition some terminal oedema and congestion of the lungs. The only significant finding was atheroma of the coronary arteries excessive for the patient's age.

Comment

Although the condition of "pituitrin shock" has been known for many years it does not seem to be widely accepted in this country that the administration of pituitrin in combination with anaesthesia (particularly cyclopropane) has any special dangers. In America, however, numerous reports of serious effects on the respiratory system—bronchospasm and increased secretion (Burstein, 1941; Greene, 1942)—and on the cardiovascular system—hypotension and arrhythmias (Adelman and Lennon, 1941; Burstein, 1941; Belinkoff, 1944)—have caused the recognition of "cyclopropane–pituitrin incompatibility," and warnings have been given both by an obstetrician (Greenhill, 1952) and by anaesthetists (Hingson and Hellman, 1951), who class it as the fifth most common cause of maternal anaesthetic death. Experimental work on the relationship of the various anaesthetic agents to the action of pituitrin has been carried out on dogs (Parsloe *et al.*, 1950). This incriminated the pressor principle as the cause of cardiac irregularities, and further demonstrated that these occurred in conscious or lightly anaesthetized subjects: deep anaesthesia appeared to protect against coronary constriction and arrhythmias. These workers also found that pitocin had no marked deleterious effects, and could find no definite evidence of that potentiation of pituitrin by cyclopropane suspected on clinical grounds.

From reading the reports of isolated cases purporting to show cyclopropane–pituitrin incompatibility one may sometimes feel that the fatalities or near-fatalities could be explained on other grounds; but the large number of these reports compels the belief that in the human subject, whatever may be the case in dogs, there is an unfavourable synergism which may lead to cardiac arrhythmia or arrest. Up to the present all these catastrophes appear to have resulted from the use of pituitrin or "pitressin," and writers have sometimes expressed the opinion that had pitocin been used all would have been well. But it must be remembered that the makers of pitocin do not claim absolute purity for their product, and that for every ten oxytocic units there is probably present at least half a unit of vasopressin, and gross cardiac irregularity has been reported in a patient under cyclopropane from as little as 3 units of pitressin given subcutaneously (Greene, 1942). Intravenous administration may be expected to produce a more intense effect.

Death in the case reported above can best be explained as resulting from the administration of vasopressin, albeit in a very dilute form, to a patient with an impaired coronary circulation who was in the stage of heightened vagal reflex activity associated with emergence from cyclopropane anaesthesia. The occurrence of ventricular fibrillation from the cyclopropane alone seems very unlikely. The administration had been brief (10 minutes), and in the first plane, with respiration gently assisted throughout, five minutes had elapsed from its discontinuance, and the patient had recovered sufficiently to make purposive movements of her head and arm: then cardiac arrest occurred about a minute after the start of the pitocin drip.

So far as a single case can indicate anything, this one should draw attention to the following facts: (1) that numerous fatalities have been attributed to the combination of pituitrin and anaesthesia, particularly with cyclopropane; and (2) that pitocin, though highly purified, is not entirely free from vasopressin. It is not too much to recommend that the pitocin drip should be used strictly in accordance with the accepted principles as regards rate of administration; should not be used during or immediately after anaesthesia with cyclopropane; and should be avoided in patients who may have coronary disease, which means in effect those over 40 years of age. Those using this method of treatment are ordinarily careful to avoid the danger of exciting excessive uterine contraction, but should also realize the possibility of other adverse effects on the mother.

Our thanks are due to Mr. J. G. Wigley for permission to publish the case, to Dr. D. F. Davies for the post-mortem report, and to both for helpful criticism.

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Medizinischer Literaturnachweis, published monthly since October, 1952, by the Öffentliche Wissenschaftliche Bibliothek, Unter den Linden 8, Berlin, has lately been enlarged and improved. It lists current monographs and papers on all branches of medicine. Entries are grouped under some 75 headings, and author and subject indexes are provided in each issue and cumulated annually. Russian titles are translated into German, other titles are given in the original published version, although it is intended eventually to translate Scandinavian and Romance language titles into German. Nearly 900 periodicals are indexed, and, although *Medizinischer Literaturnachweis* will not be quite so easily consulted by the English-speaking reader as the *Current List of Medical Literature*, it is a valuable alternative to the latter, especially as the Army Medical Library has found it necessary to reduce the number of journals regularly indexed in the *Current List*. The annual subscription is DM. 90.

THROMBOTIC MICROANGIOPATHY

BY

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Thrombotic microangiopathic haemolytic anaemia (thrombotic microangiopathy) is the name proposed (Symmers, 1952) for a rarely recognized condition which presents the striking combination of acute haemolytic anaemia, thrombocytopenic purpura, fever, and fluctuating neurological disturbances. The aetiology is unknown. The macroscopic appearances at necropsy are neither specific nor particularly striking, but the microscopical finding of widespread patchy thrombosis affecting minute blood vessels is characteristic. There is no evidence of inflammation and little or none of tissue necrosis. The condition may be related to the so-called collagen diseases.

Symmers (1952) gives a comprehensive review of the literature and adds a full study of two personal cases. He could find only 31 undoubted cases recorded: most of these had been published in the United States, where the condition is usually known as thrombotic thrombocytopenic purpura, and only three from this country. He had himself jointly reported one of these under the title "platelet thrombosis syndrome" (Symmers and Barrowcliff, 1951).

The case recorded here confirms the findings of previous observers but adds no new information; the intention is to give only enough detail to justify acceptance of the case as genuine and to stimulate interest in the disease in the hope that earlier diagnosis and treatment may alter the present uniformly fatal prognosis and that further studies may elucidate the aetiology and doubtful points in the pathology.

Case Report

A man aged 38 was admitted to hospital with a history of having been unable to work for six months because of ulcers on the legs. These had improved recently under treatment with propamidine cream and zinc and castor oil ointment. The present illness began one week before admission and was of sudden onset with cramping abdominal pain and vomiting. The urine became red in colour at about the same time, and, as the condition was thought to be due to pyelonephritis, sulphadimidine, 2 g. followed by 0.5 g. six-hourly, was given. This was discontinued after two days, as the urine darkened in colour and haemorrhagic spots developed around the tongue and buccal mucous membrane. Icterus of the sclerae was first noted on the morning of admission to hospital, when he was seen by his doctor because of loss of consciousness when getting out of bed.

There were no significant previous illnesses and no familial illnesses of note. His occupation was described as a "bench-worker" and did not involve exposure to any recognized hazard.

On admission he was noted to be a pallid, obese man who was gravely ill. His temperature was 99.6° F. (37.6° C.), pulse 120, and respirations 32. There was considerable icterus of the sclerae and mucous membranes together with bleeding of the gums. He was drowsy and showed poor attention, but there were no abnormal neurological signs otherwise at that time. The fundi showed no abnormality. A petechial rash was widely scattered but particularly plentiful in the axillae and groins. The Hess test was negative. There was marked scarring and brown pigmentation of the medial aspects of the lower limbs at the sites of the previous ulceration. Examination of the cardiovascular and respiratory systems revealed no abnormality other than the presence of crepitations at the left base. The blood pressure was 160/90. The liver and spleen were not palpable and there was no adenopathy.

Laboratory Investigations.—Urine: Marked trace of albumin; numerous red cells present; no casts seen. Blood: Hb, 6.4 g./100 ml.; red cells, 2,700,000 per c.mm., white cells, 15,000 per c.mm.; films showed a moderate polymorph leucocytosis with an occasional myelocyte; normoblasts were fairly numerous and red cells showed marked anisocytosis, poikilocytosis, polychromasia, and some anisochromia; Group O rhesus-positive, no atypical antibodies; Coombs test negative; platelets, approximately 90,000; bleeding-time, 6½ minutes; clotting-time, 11½ minutes (Wright's capillary method); serum bilirubin, 11.3 mg. per 100 ml.; colloidal gold, negative; thymol turbidity, 1.0; thymol flocculation, 0; alkaline phosphatase, 10 units; albumin, 4.2 g. per 100 ml.; globulin, 3.3 g. per 100 ml.; gamma globulin, 1 g. per 100 ml.; Wassermann reaction and Kahn test had been found negative on a previous occasion.

Treatment was begun with penicillin, 500,000 units intramuscularly followed by 200,000 units at three-hourly intervals. As the patient's principal illness appeared to be that of an acute haemolytic anaemia complicated by purpura, A.C.T.H., 100 mg., and cortisone, 100 mg., were given by intramuscular injection some six hours after his admission to hospital. His general condition continued to worsen, and twelve hours after admission a right-sided hemiplegia developed. This was followed by coma and death shortly thereafter.

Summary of Necropsy Findings.—An extremely obese male. Moderate icterus. Widely scattered petechial rash with some haemorrhagic areas in an otherwise unexceptional eczematous rash on the lower limbs and groins. Bone marrow of sternum and ribs appeared active, but there was no replacement of fatty marrow in mid-shaft of right femur. The serous sacs contained small effusions of clear slightly icteric fluid. The heart showed extensive subepicardial petechiae and ecchymoses with some intramural haemorrhages. A few petechiae were also noted in kidneys, none elsewhere. Moderate splenomegaly (weight 410 g.). Owing to an unfortunate misunderstanding the C.N.S. was not examined.

The microscopical findings were typical of thrombotic microangiopathy—that is, the partial or complete occlusion of numerous arterioles by hyaline or granular thrombus with a certain amount of endothelial reaction and absence of inflammatory cellular infiltration. The changes were maximal in the myocardium, but were also noted in the kidneys and spleen.

No vascular changes were apparent in the bone-marrow sections, which showed some degree of normoblastic hyperplasia and a considerable increase in megakaryocyte series, provisionally regarded as a reactive or compensatory phenomenon: the thrombocytopenia and occlusion of vessels are generally held to be due to formation of platelet thrombi, but this is not certain.

Discussion

The results of the laboratory investigations in life and the histological findings in the necropsy material conform exactly to those previously recorded, but shed no new light on the pathology of the condition.

The healed ulceration on the legs with eczematous rash may possibly have been a prodromal feature of the condition (urticarial rashes have been described), but its relevance or otherwise cannot be determined as the skin was not examined microscopically.

An allergic or sensitization basis has been suggested for thrombotic microangiopathy, so the fact of local treatment with propamidine cream and zinc and castor oil ointment is recorded, although this may well be irrelevant.

The correct diagnosis had been suggested on the clinical features and the combination of an acute haemolytic anaemia with thrombocytopenic purpura. Owing to the patient's sudden death 12 hours after admission no information was gained concerning the value of treatment in this disease. Symmers (1952) gives a full discussion of various measures that have been tried. These include penicillin (no effect), sulphonamides (useless or possibly harmful), aureomycin (no effect), and streptomycin (doubtful, probably no effect). As there is no evidence that the condition is infective in origin further trial of this line of treatment is unlikely to be of value. Anticoagulants have not been tried owing to the marked haemorrhagic tendency already present. Blood transfusion had given either transient or no benefit owing to rapid haemolysis of the transfused cells. Platelet transfusion might lessen the thrombocytopenia, but there would appear to be a risk of increasing the thrombotic element. Replacement transfusion might be worth considering in conjunction with other measures, of which treatment with A.C.T.H. or cortisone seems to be the most promising. A.C.T.H. has been tried hitherto in only one case (Meacham *et al.*, 1951), in which it may have been beneficial; the dosage given was small owing to the fear of ischaemic complications. Symmers points out that this objection may be unfounded. The place of splenectomy is doubtful, but it may be of value, perhaps as a long-term measure, if the patient could be tided over the most acute phase by other means.

Summary

A case of thrombotic microangiopathy is reported, only the sixth to be recorded in this country.

The salient features of the condition are fever, acute haemolytic anaemia, thrombocytopenia with purpura or other haemorrhagic manifestations, and fluctuating neurological signs.

The aetiology is unknown, but the morbid histology is characteristic—a widespread patchy thrombosis of minute blood vessels.

All cases so far recorded have been fatal, but earlier diagnosis would afford at least a hope of successful treatment; the condition may not be so rare as the extreme paucity of reports would suggest, and it should be considered in any case of febrile jaundice with haemorrhagic features.

Extensive reference has been made to a comprehensive paper on the subject which is readily accessible (Symmers, 1952).

We wish to thank Dr. J. C. Heather for permission to publish and Professor W. St. C. Symmers for confirming the histological diagnosis. Dr. T. Baird kindly supplied details about the patient before his admission to hospital.

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At the annual general meeting of the Medical Sickness Finance Corporation Ltd., held on April 27, it was reported that, during 1953, 1,153 agreements were entered into for a total of £417,777. This was an increase on the previous year's business, and the corporation continues to expand. Although the largest demand was for motor-cars, agreements were also completed for caravans, motor cycles, electrocardiographs, *x*-ray apparatus, surgery furniture, and other medical equipment. The Corporation is a subsidiary of Medical Sickness Annuity and Life Assurance Society Limited, and Sir CECIL WAKELEY, P.R.C.S., is chairman.

MALIGNANT DISEASE ASSOCIATED WITH VASCULAR PHENOMENA

BY

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Trousseau (1877) drew attention to recurring phlebitis as the first sign of obscure visceral carcinoma. He pointed out that it may be diagnostic in certain cases, and that it may occur with cancer affecting any internal organ. To the present date 60 cases of thrombophlebitis migrans associated with carcinoma have been reported.

Wright (1952) mentions that he has seen 20 such cases, but does not report them in detail. He observes that the diagnosis of malignancy must be suspected (*a*) whenever thrombophlebitis persists, or is migratory, in spite of adequate anticoagulant therapy in adults over 30, and with increasing suspicion in the older age groups; and (*b*) when there is unexplained bleeding with prothrombin times in the therapeutic (not excessive) range. Gross *et al.* (1951) reviewed the literature of reported cases up to 1951. Of these cases, 10 were associated with carcinoma of the stomach, 32 with carcinoma of the pancreas (head, body, and tail), 9 with lung cancer, 2 with gall-bladder cancer, 1 with carcinoma of pancreas or stomach, and 2 were undetermined. A further four cases associated with carcinoma of the lung have been reported by Fisher *et al.* (1951).

Raynaud's phenomenon associated with malignant disease is rare, and only three cases are reported in the literature (Pasteur and Price Jones, 1901; Hamilton, 1920; Bennett and Poulton, 1928).

The object of this paper is to report four cases of malignant disease presenting as thrombophlebitis migrans and one case presenting with Raynaud's phenomenon, and to discuss the possible relationship and pathogenesis.

Case 1

A man aged 35 was admitted to hospital on September 2, 1951, with a history of vague malaise for seven months. Five weeks previously he had developed a thrombosis of the superficial veins of the left arm. Twelve days before admission thrombophlebitis in the left leg developed, associated with haemoptysis five days later. During the course of his illness until his death further episodes of haemoptysis occurred, the radiological appearances being compatible with pulmonary infarcts. At various times thrombophlebitis occurred in the left leg, right leg, superficial abdominal veins, dorsum of the right hand, and left external jugular vein.

Three months after admission a right-sided pleural effusion developed. Malignant cells were identified in the pleural fluid, indicative of a bronchogenic carcinoma. The liver became enlarged and nodular, and he died on January 2, 1952.

Anticoagulant therapy with ethyl biscoumacetate ("tromexan," 4-hydroxycoumarin) was maintained during his whole illness until December 22. The maintenance dose varied between 300 and 450 mg. daily, the prothrombin concentration being kept at 10 to 25%, with occasional escapes. In spite of this, thrombotic episodes occurred even with a prothrombin concentration of 10%.

Case 2

This patient, a man aged 46, was admitted to hospital on March 8, 1952. One month previously thrombophlebitis

occurred in the left leg. Sudden pain in the left side of the chest with dyspnoea and coughing of blood-stained sputum occurred on the day of admission.

During the course of his illness until his death on December 14 thrombophlebitis migrans occurred in both arms, superficial and deep veins of both legs, superficial veins on the abdominal wall, the corpus cavernosum, and finally the inferior vena cava. There were also recurrent episodes of pain in the chest, dyspnoea, and haemoptysis, and radiographs at these times showed lesions in the left mid-zone, left upper zone, left base, and right base respectively, all of which appeared to be compatible with pulmonary infarcts. Terminally, gross radiological changes occurred in the chest, particularly elevation of the left diaphragm due to involvement of the left phrenic nerve by neoplasm. Extensive investigations, including bronchoscopy on two occasions, failed to reveal a primary neoplasm.

A thrombophlebitic lesion on the abdominal wall did not resolve as the other lesions had, and gradually increased in size. This was removed for biopsy on September 9, and showed a secondary deposit from an adenocarcinoma. Vein biopsy had been done previously: on April 17 biopsy showed a simple venous thrombus, the vein wall being normal. A further biopsy on May 10 showed blood clot in the lumen of the vein. There was an intramural cellular reaction containing some cells of unidentified origin, ? malignant cells.

Treatment with ethyl biscoumacetate was begun on admission. The dose varied between 300 and 1,500 mg. daily to maintain a prothrombin concentration of 10 to 25%. The anticoagulant was changed to phenylindanedione ("dindevan") on August 2, and was continued until November. While the patient was on anticoagulants, rectal haemorrhage occurred at the same time as a thrombotic episode.

Post-mortem Examination (December 15).—The lungs contained a few hard nodules with reddish centres which were healing infarcts. In the right stem bronchus was a primary bronchogenic carcinoma. Secondary deposits were present in the mediastinum, the left suprarenal gland, and the liver. The other organs were normal. Numerous sections of veins did not reveal any malignant cells in the lumen or the wall of the veins; neither were malignant cells seen in the pulmonary infarcts.

Case 3

This patient, a man aged 43, was admitted to hospital on December 10, 1953. Four months previously thrombophlebitis occurred in the left leg. This was followed in a few weeks by a similar episode in the right leg. Later, a troublesome cough and haemoptysis developed, and thrombophlebitis occurred in the right arm. At the time of admission his condition was poor. Thrombophlebitis was present in the right arm and both legs; these were new lesions. A radiograph of the chest showed congestion at the right base.

Bronchoscopy on December 14 revealed a bronchogenic carcinoma partly occluding the bronchus. Biopsy confirmed the diagnosis. His condition deteriorated rapidly, with the development of secondary deposits in the liver, and he died on January 7, 1954. Permission for a post-mortem examination was refused.

Case 4

A man aged 63 was admitted to hospital on April 9, 1953, complaining of abdominal pain, loss of weight, and recent onset of jaundice. He had been perfectly well until December 5, 1952, when he developed pain in his right thigh due to thrombophlebitis. This resolved in the ensuing weeks, but was followed by a similar episode in the left leg. The thrombophlebitis in the left leg resolved in three weeks. A further thrombotic episode occurred in the right leg, associated with a chill, a stabbing pain in the chest, and a cough. This cleared up quickly. There were no further thrombotic episodes. In February, 1953, he developed umbilical pain, constant in character and associated with paroxysms of more severe pain. During the next six weeks his condition deteriorated, with progressive loss of weight and weakness. Jaundice developed two weeks before admission to hospital.

At the time of admission he was cachectic and jaundiced. The liver was a little enlarged. Palpable glands in the left side of the neck, consistent with malignant deposits, were noted. It was considered that this patient had secondary carcinomatosis. His condition deteriorated, and he died on April 27.

Post-mortem Examination (April 28).—The main findings were a mass of secondary carcinoma in the tracheobronchial angle. The liver was somewhat enlarged and was bile-stained. There were no secondary deposits in the liver. In the head of the pancreas was a large mass obstructing the common bile duct. Secondary deposits were present in the glands at the root of the mesentery. The other organs were normal. The histological appearance of the carcinoma of the head of the pancreas was that of an anaplastic carcinoma.

Case 5

A bank cashier aged 54 was admitted to hospital on November 23, 1951, complaining that his fingers had become blue and painful. The onset had been quite sudden, occurring three weeks previously, when the patient was out in the country engaged in sport. Pain and throbbing had become persistent and more severe in the ensuing weeks.

On admission the only abnormal findings were that both hands were cold and blue from the mid-palms to the finger-tips, with commencing gangrene of all the finger-tips on both hands. Radiographs of the cervical spine and chest were normal. The blood count was normal, and no haemagglutinins were detected. The Wassermann and Kahn reactions were negative. An electrocardiograph was within normal limits.

Treatment with tolazoline hydrochloride ("priscol") produced a definite warming of the hands with return to normal colour, except for the fingers, which remained white and the tips blue.

A cervical sympathectomy (Mr. E. W. Grahame) was performed on the right side on December 6. Although Horner's syndrome was produced there was no improvement in the fingers. The small gangrenous areas separated satisfactorily and the patient was discharged from hospital on December 23. He was readmitted on March 10, 1952, complaining of loss of appetite and nausea. Raynaud's phenomenon had not improved. A barium meal examination showed a small hypertonic stomach with an atrophic mucosa and rapid emptying. No ulcer or filling defect was noted. His general condition was unchanged and he was discharged on March 28. One month later he was again admitted. There had been persistent vomiting and marked loss of weight. He was now cachectic. A large craggy mass was palpable in the upper abdomen, which was thought to be an inoperable carcinoma of the stomach. He died one week later.

Post-mortem Examination.—On May 8 necropsy showed extensive carcinomatous deposits in the abdominal cavity arising from a primary carcinoma of the stomach. The other organs were normal. A portion of the thumb was taken for histological examination. This showed no evidence of arteriosclerosis or endarteritis.

Discussion

Sproul (1938) investigated the frequency of multiple venous thrombosis associated with carcinoma of the body or tail of the pancreas. In only a small number of this post-mortem series were malignant cells identified in the vein wall. She suggested that an increase in pancreatic secretion might increase the quantity of prothrombin in the blood, and this, with the tumour cells in the blood stream, might initiate the formation of thrombi.

Kenney (1943), Edwards (1947), and Gross *et al.* (1951) all implicated an altered clotting mechanism, due to various factors, as responsible for thrombophlebitis migrans in this syndrome.

It has been suggested that estimation of the coagulation power of the blood may be an aid in the diagnosis of cancer (Bock and Ransche, 1926). The results, however, are contradictory (Van Allen, 1927; Perlmann and Rodin, 1927). The reports of these authors were prior to the use of anticoagulant therapy. The failure of anticoagulant therapy to control these thrombotic episodes even with dangerously low prothrombin concentration indicates that altered blood coagulation is not an adequate explanation.

Raynaud's phenomenon associated with malignant disease is rare. Bennett and Poulton (1928) suggested that in their case it was due to a malignant gland invading the right inferior cervical ganglion. Raynaud's phenomenon, however, was bilateral. In Case 5 no secondary deposits were found above the diaphragm.

Coman (1953) discussing blood-borne tumour metastases, points out that direct dissemination of cancer cells depends mainly on their entrance into the vascular channels, and that the size of the emboli vary from single cancer cells to fairly large clumps. It is also known that cancer cells have amoeboid properties and can invade tissues, including the walls of the veins.

It is suggested, therefore, that both thrombophlebitis migrans and Raynaud's phenomenon, when associated with malignant disease, are due to emboli of malignant cells. The size of the emboli determines the site in which they settle: in the lungs, causing pulmonary infarcts; in the digital arteries, resulting in Raynaud's phenomenon; or in the peripheral veins, causing thrombophlebitis. In most cases the emboli are small, and the formation of a thrombus around the malignant cells results in the death of these cells. This is the commoner event. Occasionally, this does not occur, and a metastatic deposit can then be observed to develop.

Summary

Four cases of thrombophlebitis migrans associated with carcinoma are reported. In three cases the primary growth was in the lung; in the fourth it was in the head of the pancreas.

One case of Raynaud's phenomenon with carcinoma of the stomach is reported.

Attention is drawn to the fact that, when thrombophlebitis migrans is not adequately controlled by anticoagulant therapy the possibility of an underlying carcinoma must be considered.

It is suggested that the mechanism is due to emboli of malignant cells and that there is no underlying alteration in blood coagulation.

I wish to thank Dr. S. Wray, Director of the Central Clinical Laboratory, Middlesbrough, for the pathological studies, and Mr. E. W. Grahame, consultant surgeon, Tees-side Hospitals.

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FACIAL DIPLEGIA IN THE GUILLAIN-BARRÉ SYNDROME

BY

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The Guillain–Barré syndrome, or acute infective polyneuritis, has aroused much interest in recent years. It is still a matter of discussion whether or not it is a disease *sui generis*, and recent opinion seems to favour a diverse aetiology for the syndrome. Laurans (1908) published the first adequate review of the condition, emphasizing the widespread flaccid paralysis and the facial diplegia. Guillain *et al.* (1916) did not recognize the facial diplegia as part of the syndrome, and it was not until 1936 that Guillain admitted the frequency of this form of paralysis. Holmes (1917) described cases in soldiers which were obviously of this syndrome, and Bradford *et al.* (1919) published a series which included 17 cases with involvement of the seventh nerve. Petch (1949) gives an excellent review of the subject, stating that the aetiology is unknown and the infective nature unproved. He described eight cases, in two of which bilateral facial paralysis (facial diplegia) had occurred. Bannwarth (1949) regards the condition as a parallergic process which may occur in a great variety of diseases, and Shaby (1949) also takes the same view of its multiple aetiology. Other authors hold the opinion that it is primarily an infective process of unknown, probably virus, aetiology—hence the name "infective neuronitis" used in American literature. McIntyre (1937) and de Jong (1940) indicate three groups—acute cases ending in recovery; cases running a protracted course, often with development of permanent paralysis; and cases terminating fatally, usually with bulbar paralysis.

The present report includes six cases, all females, who developed bilateral facial paralysis. Four of these were seen before paralysis of the face or body had developed, and the principal reason for reporting them is the observation, not hitherto recognized, that in the early stages the deep tendon reflexes are exaggerated. It is maintained from observation of these cases that it is possible to diagnose the condition in the pre-paralytic phase, and in three of the cases the development of facial diplegia was forecast before the onset of paralysis. Diagnostic points in the *early* stage of the disease are intense paraesthesiae, beginning in the feet, hands, and limbs, and spreading in severe cases all over the body. One patient said she felt as if she had "passed through fire." At the same time, pain is experienced in the muscles of the limbs, mainly in the proximal groups; pain in the eyes is common; and on clinical examination exaggeration of the deep reflexes is present, with no objective sensory change, and there is muscle tenderness on pressure; later the deep reflexes disappear and varying degrees of paralysis ensue. Four of these six cases had a preceding febrile illness six to thirteen days previously. A differentiating point from poliomyelitis is the widespread tenderness, which is bilateral and symmetrical, and as a rule principally affects the proximal groups of limb muscles.

Case 1

A married woman aged 36 was seen at home on July 20, 1948. Six days previously she had developed a right facial paralysis with inability to taste. Her eyes were aching, and

she had had a headache and pain in the back of the neck and shoulders. Her legs felt sore to the touch and her bowels had not been opened for five days. She had found difficulty in talking. There had been no sore throat. On the morning of the 20th she developed a left facial paralysis, which was probably the reason for her difficulty in speaking, although she herself had not noticed that the left side of the face was paralysed.

On clinical examination there was bilateral facial paralysis with inability to close both eyes. She could not raise her legs from the bed, and dorsiflexion of the feet was poor. The arms could not be raised and there was a poor grip in both hands. Muscle tenderness was pronounced in the thighs, in the anterior tibial group, in both calves, and in the trapezius and deltoid on both sides. The deep reflexes were absent in all four limbs : there was no apparent sensory loss or any neck rigidity. Examination of the eyes showed full eye movements, but the pupils did not react to light or on accommodation.

She was admitted to hospital, where a lumbar puncture on July 22 showed : pressure, 140 mm. ; protein, 120 mg. per 100 ml. ; no cells. A blood count was normal. She had a persistent fever until August 10 ; it then gradually settled. The reflexes returned to the arms in a few days, being present on July 23, and by the end of September the knee-jerks had also returned. Within a month the right side of the face had recovered, although the left side was still weak. A further lumbar puncture on August 12 showed protein, 40 mg. per 100 ml., and 80 lymphocytes per c.mm. She eventually made a complete recovery, and has had no further neurological symptoms since.

Case 2

A married woman aged 27 was admitted on November 23, 1948. Thirteen days previously she had had a febrile attack with a little temperature, and felt ill. Six days before admission she had felt pain between the scapulae, which became worse over the next two days ; she then developed severe headache, and this had persisted up to the time of examination. She had had tingling in the legs three days before admission, and on the morning of the 23rd she woke with the left side of the face paralysed. There was numbness down the left side of the body, more marked in the left leg, and she said the bedclothes felt cold.

On clinical examination she was nervous, with a heart overacting at 100, and had a complete left facial palsy and a partial right facial palsy, affecting the upper half of the face. There was no obvious motor or sensory loss at this stage, but the thigh muscles and shoulder-girdle muscles were tender on pressure. The left knee-jerk was brisk and the right normal. Both ankle-jerks were absent. The plantar reflexes were flexor.

She ran a temperature up to 100° F. (37.8° C.) for three days. A lumbar puncture on November 29 showed protein 50 mg. per 100 ml., and no cells. A blood count was normal. No further paralysis developed, but the facial paralysis persisted, and, although there was a gradual recovery, she still had weakness of the left side of the face in July, 1949. In February, 1950, she was still conscious of a little weakness of the left angle of the mouth.

Case 3

A married woman aged 35 was admitted on February 21, 1949. She had had an occipital headache for a fortnight, and four days before admission had had pains in the legs, spreading up into the back and into both arms. She had had tingling in the feet and legs, and for two days had repeated vomiting.

When first seen she was tender in the muscles of the calves and thighs and in the deltoids ; the right knee-jerk was absent, but the other deep reflexes in the arms and legs were brisk. A lumbar puncture on February 22 showed normal pressure, 140 mg. protein per 100 ml., and 15 cells, all lymphocytes.

On February 28 she complained of numbness in the arms, her hands felt weak, the arm reflexes were now absent, and the left knee-jerk was also sluggish. All arm muscles were tender on pressure. Three days later she developed a bilateral facial palsy, more pronounced initially on the left side, but by March 7 it was complete. All her deep reflexes were now absent. She had severe pain in the arms and legs, with loss of power in the shoulder-girdle, pelvis, and thigh muscles. At the end of March her facial movements were returning and the limb movements were stronger. In April her deep reflexes gradually returned and she made a complete recovery. A year later, however, she still complained of some numbness in the feet.

Case 4

A married woman aged 21 was admitted on October 4, 1950. Six days previously the tips of her fingers and toes felt numb, and this gradually spread over the body. Movement of any muscle caused pain. Three days later she had bitemporal headache with a feeling of pressure on the eyes. She could not open the mouth properly, and had some photophobia. She vomited on the day of admission. There had been no preceding sore throat or febrile illness.

On examination she had marked tenderness in the muscles of the arms, forearms, thighs, and calves, and in the masseters and temporal muscles. She was unable to open her mouth or to articulate properly. Limb movements were normal, with no apparent loss of power, although movements were painful. The triceps-jerks and biceps-jerks were absent, and at this stage the knee-jerks and ankle-jerks were both brisk ; the plantar reflexes were flexor, and there was no sensory loss to pinprick or to cotton-wool or vibration sense. The optic fundi were normal, but she had pain on trying to look up. Her facial movements, apart from inability to open her mouth, were normal. A blood count showed nothing abnormal.

The following morning there was weakness of the left side of the face ; this became complete by the evening, and the next morning there was bilateral facial palsy. She rapidly developed weakness of the arms and legs, the pain in the limbs increased, and by the end of the third day after admission, coincident with the onset of paralysis, the deep reflexes disappeared. With this widespread paralysis there was fear that diaphragmatic paralysis might ensue, so she was transferred to the isolation hospital.

Within 24 hours diaphragm movements became weak and she was placed in an iron lung, but the movements returned within 48 hours and she was taken out of the lung. The paralysis of the limbs, however, persisted.

She was readmitted to Harefield Hospital on October 16, 1950. The muscle tenderness was now very much better and she was feeling well in herself, but said that her hands felt like "two wet fish." She was still unable to chew, but could swallow with no nasal regurgitation. She now had some loss of light touch sensation and to pin-prick over her finger-tips.

By October 23 movements began to return in the arms and the lower lip. On November 1 there was a slight movement of the right side of the face. By the 14th she could use her limbs and could feed herself. From this time recovery was rapid, and by December 18 muscle recovery was complete, except for slight weakness in the left upper facial muscles. Within a month this had also recovered completely.

She was subsequently seen at intervals over the next two years, when there was no sign of recurrence.

The C.S.F. findings were of interest : October 5 : cells less than 1 ; protein, 190 mg. per 100 ml. ; chlorides, 740 mg. per 100 ml. November 6 : red blood cells, 3 ; white blood cells, 1 ; protein, 240 mg. per 100 ml. ; sugar, 72 mg. per 100 ml. November 21 : pressure, 200 ; 2 lymphocytes, 3 red blood cells ; protein, 210 mg. per 100 ml. ; Lange 2111000000. December 4 : clear colourless fluid ; pressure, 160 ; 3 white blood cells ; protein, 300 mg. per 100 ml. ; Lange 1221111100.

Case 5

A married woman aged 47 was seen at home on July 16, 1952. Thirteen days previously she had a febrile illness diagnosed as influenza. Ten days later diffuse irritation occurred all over the body. The following day her eyes hurt on movement, and that night she had pain in the arms and legs—it felt as if it was "in the bones." The following morning she still had the pain, and found she could not read small print. During the course of the day the irritation of the skin increased. She felt "as if she had passed through fire." Trembling fits occurred which she could control voluntarily.

On the morning of July 16 she had diplopia, which had persisted. She had had retention of urine for seven hours, but later passed urine with difficulty. Her appetite was poor and she vomited once.

Clinically she complained of diplopia on looking to the left and blurring of vision on looking to the right, but there was no obvious ocular palsy or nystagmus; the optic fundi were normal, and the visual fields were not restricted. Her speech was normal, but her doctor and her husband commented that cerebration was slower. There was no loss of power in any limb, but the muscles were tender on pressure in the thighs, calves, and arms. All her deep reflexes were exceedingly brisk. The plantar reflexes were flexor. Apart from a doubtful loss to pin-prink sensation on the legs, there was no sensory change. The heart rate was 130 and regular, the heart sounds were normal, and the blood pressure was 135/95. A blood count was normal, and also the urine.

She was admitted to hospital, where she was found to have a raised C.S.F. pressure, 90 mg. of proteins per 100 ml., and fewer than 5 cells per c.mm.

Two days after admission she developed generalized weakness of all limbs, together with poor diaphragm movements, and was transferred to the isolation hospital. Her deep reflexes became sluggish, but did not disappear, and at the same time she developed bilateral facial palsy. The respiratory paralysis did not develop, and she was transferred to Harefield Hospital. A further lumbar puncture on July 27 showed: protein, 80 mg. per 100 ml.; 1 lymphocyte per c.mm; chlorides, 750 mg. per 100 ml.; Lange 0000000000. She improved rapidly, and was discharged on August 5, having completely recovered all facial and limb movements.

Case 6

A married woman aged 42 was admitted to the isolation hospital on July 30, 1953, with a history of pain behind the eyes and left facial palsy for two days. Six days previously she had had some pain in the back with general malaise. On the day before admission she developed a right facial palsy also. She had tingling in the hands and feet, but no other symptoms. On admission there was bilateral facial palsy, eye movements were full and normal, and muscle power was normal in all limbs. The ankle-jerks were absent, but knee-jerks were brisk. Within two days all her deep reflexes except the triceps-jerks disappeared. Lumbar puncture showed 110 mg. protein per 100 ml., and 1 polymorph cell only. Her blood count was normal.

She was transferred to Harefield Hospital on August 4. By this time, however, her deep reflexes had returned, though they were sluggish, but the ankle-jerks were still absent. Repeat lumbar puncture on August 17 showed 65 mg. of protein per 100 ml., and no cells. Recovery of facial movements was very slow, and she was discharged home on September 12 with a little but still incomplete movement of the face.

Treatment

No specific treatment was given other than physiotherapy when the acute stage had subsided.

Summary

Six cases of the Guillain–Barré syndrome are described. All had facial diplegia. In four of them, exaggeration of deep reflexes was observed in the pre-paralytic stage. Paraesthesiae and bilateral muscle tenderness followed by widespread paralysis of limbs were a feature in five of the cases.

I am grateful to Dr. J. T. Scott and Dr. A. Stuart for their help with these cases, and in particular to Dr. V. Lambert, of St. John's Isolation Hospital, for his willing help and co-operation at all times.

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Medical Memoranda

Sudden Simultaneous Arterial Embolism Involving All Four Limbs

The following case is unusual enough to merit recording.

CASE REPORT

A man aged 58 was admitted to hospital complaining of difficulty in passing water. There was a history of a urethral discharge some 30 years previously, followed by a course of injections in the buttock, but no history of venereal sore. He had remained well until some 12 months before admission, when he noticed progressive difficulty in passing water. The stream got smaller and smaller and eventually stopped. At this point he attended a V.D. out-patients department, where a diagnosis of urethral stricture was made and his urinary retention was relieved after the passage of a curved sound. A blood W.R. taken at this time was found to be positive (strong). He did not attend for further treatment until retention occurred a second time some six months later. Instruments were again passed, after which he voided about 18 oz. (510 ml.) of urine loaded with pus. He was admitted to hospital the following day.

Examination revealed a rather pale ill-looking man. The presence of a stricture in the bulbous urethra was confirmed instrumentally; slight bleeding followed the passage of a medium-sized curved sound. Shortly afterwards, prior to a more detailed physical examination, he had a syncopal attack when paying a visit to the toilet. Loss of consciousness was brief: he was seen by a medical officer within a few minutes and ordered strict rest in bed, warmth, and copious fluids. During the afternoon his temperature rose to 102° F. (38.9° C.), but his general condition was described as satisfactory.

The next day he seemed to have recovered from his syncopal attack. There was hardly any urethral bleeding, and urine was passed quite satisfactorily. He was ordered to remain on strict rest in bed and to take copious fluids. His condition was satisfactory for the next five days, but the following night he complained to the nursing staff that his limbs had suddenly become painful, and on examination they were found to be discoloured.

Examination early the following morning showed a very ill-looking man with a dry brown tongue and labial herpes. Both hands and both forearms were cold and cyanosed and completely pulseless. Arterial pulsation could be felt in both antecubital fossae, but none at all below this level. Both legs were similarly cold and pulseless: the skin of the right leg was mottled blue and white; mottling was not present

on the left side. Arterial pulsation could be felt above the inguinal ligament but not below this level; the left femoral artery could be felt pulsating for a short distance below the inguinal ligament. It was impossible to detect pulsation in either popliteal fossae or at any point below this level. The skin of the scrotum was also deeply cyanosed. The patient was conscious and quite rational. The heart seemed to be beating strongly: a systolic murmur could be heard at the apex. There were rales at both lung bases. The colour and temperature of the skin of the trunk were normal.

A diagnosis of multiple arterial embolism was made: the prognosis was very poor if not hopeless, but death occurred sooner than was anticipated. The patient suddenly developed Cheyne–Stokes respiration and died within a matter of minutes a few hours after being examined and before any pathological examinations had been carried out.

POST-MORTEM REPORT

A post-mortem examination was made the following day, about twenty hours after death. The body was that of an elderly male. Sordes was present on the mouth. An infarct, which appeared to be of fairly recent origin, was found in the wall of the left ventricle: it did not involve the endocardial surface of the ventricle, which was of normal appearance, and no intracardiac thrombus was seen. Careful examination of the heart valves showed them to be normal. The coronary arteries and their main branches were laid open, but the expected thrombus was not found.

Striking changes were present in the ascending aorta and aortic arch. Projecting into the vessel lumen were several large exuberant thrombi attached to the base of atheromatous ulcers. The adventitia was thickened, and subsequent histological examination showed focal collections of lymphocytes and ruptured elastic fibres, suggesting the coexistence of both aortic syphilis and atheroma. No aneurysm was present.

A detailed dissection of the right femoral artery revealed an embolus with propagated thrombus extending to within 5 in. (12.5 cm.) of the inguinal ligament. There were signs of a diffuse infection in both lungs and a considerable amount of purulent material in the main bronchi.

The right kidney was scarred as a result of previous pyelonephritis; the left was normal apart from a recent infarct at the upper pole. The right ureter was dilated; the bladder showed cystitis with periureteric diverticula. A stricture was present in the bulbous urethra.

Cirrhosis of a coarse nodular type was present in the liver. The brain was oedematous, but no gross vascular lesion was found. Examination of the gastro-intestinal tract, thyroid, and adrenals revealed no lesion of any significance.

DISCUSSION

Whereas the clinical picture left one in no doubt that emboli had lodged in all four main limb vessels, it was only at necropsy that the source of the emboli was revealed.

Aortic atheroma is a notoriously "silent" lesion, and in consequence is given far greater prominence in textbooks of pathology than in textbooks of medicine. Despite its frequency as a post-mortem finding, it is unusual for the swift arterial current to allow thrombi of any size to build up on the aortic wall even in advanced cases of atheromatous ulceration. Still less commonly do such thrombi become detached to block an artery farther down the vascular tree and cause clinical symptoms. Thus Kvale (1947), in an analysis of 100 cases of arterial occlusion studied at the Mayo Clinic, does not list it as an aetiological factor. It is possible, however, that cases do occur and masquerade under the diagnosis of arterial thrombosis. Learmonth (1948) describes cases in which an embolus has originated from a mural thrombus in a large artery.

In discussing the subject of multiple embolism a distinction must be drawn between multiple emboli occurring consecutively and multiple emboli occurring simultaneously. A succession of arterial emboli may punctuate the course of a number of diseased states, notably subacute infective endocarditis and auricular fibrillation.

On the other hand, multiple embolism occurring simultaneously has very rarely been recorded. Branch (1937) describes the case of a man aged 56 with a 10-years history of hypertension who developed simultaneous occlusion of both popliteal arteries. He lived for five days, during which time the occlusion spread proximally to both femoral arteries. Permission for a post-mortem examination was refused. Branch speculates on the cause, and observes that the literature mentions no previous case of simultaneous obstruction of the arteries of the lower extremities of sudden onset. Fiddian (1949) records the case of a man aged 69 who developed simultaneous embolism of both axillary arteries two and half months after a leg amputation. He does not suggest any source for the embolism, and no references are cited. I have been unable to trace any previously recorded cases of simultaneous occlusion of all four limb arteries.

My thanks are due to Dr. H. E. Vickers, consultant pathologist, Walton Hospital, for the post-mortem examination and for permission to summarize the post-mortem report.

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Contamination of Streptomycin Solutions with Resistant Bacteria

The recent coincidence of abscesses at the site of injection of streptomycin in three different patients under treatment for tuberculosis has drawn our attention to what is likely to be an increasing hazard of chemotherapy. Records of the hospital concerned showed that 10% of the patients given courses of streptomycin for tuberculosis in the previous five years had suffered from a similar abscess. Pus from the abscesses had been cultured in most instances, yielding growths of *Staphylococcus aureus*. The earlier cases of sepsis had appeared sporadically, so that their significance was overlooked, but it was now obvious that inquiry was necessary into the methods used for preparing and injecting the streptomycin.

Solutions of streptomycin were prepared the day before use by adding 2 ml. of sterile water to 1 g. of the base (as the calcium chloride compound). Samples of such solutions were taken for culture by inoculating 5-ml. volumes of broth with two or three drops from syringes charged ready for injection. The bottles of broth were then posted to the laboratory. After incubation for five days, 6 out of 27 such samples yielded a growth of *Staph. aureus*. Swabs of equipment and materials yielded no pathogenic staphylococci. Two nurses shared the task of dissolving and injecting the streptomycin. One of them, Nurse A, proved to be a heavy nasal and skin carrier of *Staph. aureus*, and the other, Nurse B, a nasal carrier. The strains isolated from the three most recent abscesses, the streptomycin solutions, and the two nurses were typed with bacteriophage and their sensitivity to five antibiotics determined. All except one belonged to phage-type 53/77 and were resistant to streptomycin and penicillin but sensitive to aureomycin, oxytetracycline, and chloramphenicol. The exception was the strain isolated from Nurse B, which belonged to type 52A and was sensitive to all five antibiotics.

The survival of two of the streptomycin-resistant strains was studied in streptomycin solutions of 300,000 units per ml. When 10^8 viable cocci were added to 1 ml. of solution 25% survived after 24 hours at room temperature in the dark. With 10^8 cocci per ml. approximately 1% survived in the same conditions. In contrast, similar tests on streptomycin-sensitive staphylococci with an inoculum of 10^8 per ml. showed that more than 99% were killed in 10 minutes, a finding consistent with the observations of

Garrod (1948). Streptomycin sulphate and the calcium chloride compound behaved similarly in these experiments.

Following improvements in the dispensing and injection technique, 75 samples of streptomycin solution proved sterile on culture. We attribute this result, however, not so much to any specific changes in technique as to greater care having been taken when the hazard was understood. It seems advisable to impress on novices and occasionally to remind experienced staff that antibiotic solutions may not be self-sterilizing and that therefore they always require a rigorously aseptic technique in their use. Stable ready-prepared solutions of streptomycin have recently become available commercially, and these should reduce the danger of contamination, besides saving labour and lessening the risk of drug sensitization of staff. Samples of such a solution containing 0.25% phenol were examined. Little bactericidal action was observed over a period of 10 minutes with inocula of 10^6 streptomycin-resistant cocci per ml. of solution, and care therefore should not be relaxed even when such products are used.

We are indebted to Dr. R. E. O. Williams, of the Central Public Health Laboratory, Colindale, for carrying out the bacteriophage typing.

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Torsion or Spontaneous Haemorrhagic Infarction of Testicle in Newborn Infant

In the newborn infant the scrotum is sometimes abnormally swollen or red, this occurring most commonly after breech deliveries. The condition is assumed to be bruising of the scrotum during delivery, and usually subsides satisfactorily. Swelling of the scrotum is also occasionally seen after normal deliveries, and may be due to syphilis, tumours, torsion of the testicle, or spontaneous haemorrhagic infarction of the testicle. Congenital syphilis is becoming rare owing to routine antenatal supervision and treatment; therefore syphilis of the testis in the newborn is also increasingly rare. Tumours seldom occur at this age: the literature is comprehensively reviewed by Campbell (1951). In a review of 95 cases of testicular tumour by Hickinbotham (1950) the youngest patient was 13 months old.

Attention has recently been drawn to the occurrence of torsion of the spermatic cord, and spontaneous haemorrhagic infarction of the testicle in the newborn. Spontaneous haemorrhagic infarction of the testicle was first described as a separate entity by Campbell (1937) and later by MacLean (1943) and Ravich (1947). From the description given by Campbell it appears that there is no way of distinguishing between torsion and spontaneous haemorrhagic infarction of the testicle except by exploration at operation. Campbell assumed that as no torsion was found at operation the infarction had been spontaneous in his cases. On the other hand, it might be postulated that there had been a twist which had become undone while the gangrene remained. Against this theory is the fact that oedema and fixation of the testis occur very early when there is torsion, as shown by Ownby and Atkinson (1942). It may be assumed, therefore, that very occasionally infarction of the testicle does occur spontaneously, though most cases are secondary to torsion.

CLINICAL FEATURES

The clinical features of these two conditions appear from the published descriptions to be identical. The child is born with a red, swollen scrotum, the skin seems to be oedematous and is often adherent to one testicle, which appears to be the affected organ. In those cases in which torsion occurs in a fully descended testis it is reasonably easy to exclude the possibility of a strangulated inguinal hernia by finding that the tumour is circumscribed above.

Some authors (James, 1953) stress the fact that the child's general condition may not be disturbed at all: there may be no increase in the pulse rate, no rise of temperature, and no pain or tenderness. Further detailed examination of these cases does not seem to produce any useful information. After diagnosis the main problem is treatment.

We have traced four cases of spontaneous infarction of the testicle in the newborn as described by Campbell, Ravich, and MacLean. All were explored and in each case orchidectomy was performed. James, in a very complete analysis of the literature, traced six cases of torsion of the testis occurring in the neonatal period and added a seventh, one of the two cases reported in his paper. In all these cases the testicle was removed sooner or later within the first few weeks of life, and one of the babies died from gastro-enteritis while still in hospital.

Two cases seen recently by us fulfilled the clinical criteria of either torsion or spontaneous infarction of the testis in the newborn.

CASE REPORTS

Case 1.—Mother aged 28, healthy. First child. Pregnancy uneventful; full term. Labour normal, vertex presentation. Length of labour: first stage, 10 hours; second stage, 1 hour 5 minutes; third stage 20 minutes; total duration, 11 hours 25 minutes. Birth weight, 10 lb. 1 oz. (4,560 g.). At birth the child was found to have a swollen red mass in the left side of the scrotum. The diagnoses considered were syphilis, new growth, and torsion. The first was ruled out by serological tests, the second by subsequent progress. The third was regarded as a possibility in spite of the fact that there was no local tenderness, no rise in temperature, or any constitutional upset. The condition gradually subsided and the testicle became smaller, until now, at the age of 2 years, it is no larger than a split pea.

Case 2.—Mother aged 27, healthy. Two previous pregnancies, eight and four years earlier—birth weights, 7 lb. 6 oz. (3,345 g.) and 8 lb. 3 oz. (3,715 g.). Pregnancy of present case normal. Labour normal, vertex presentation. Length of labour: first stage, 4 hours 10 minutes; second stage, 25 minutes; third stage, 30 minutes; total duration, 5 hours 5 minutes. Birth weight: 8 lb. 13 oz. (4 kg.). At birth the right side of the scrotum was found to be red, swollen, and hard. It did not seem to be tender, and there was no rise of temperature. After two days the testicle was seen to be adherent to the scrotum. This adherence gradually disappeared, and no suppuration occurred. The baby made excellent general progress and has been followed up for eight months. The testicle has gradually become smaller, and is now about the size of a small pea.

COMMENT

We do not think that surgical treatment as reported in the published cases has brought any particular benefit to the patients. They have been submitted to a general anaesthetic in some cases, to a local analgesic in others, and in each case to an operation at an early age. All have lost their testes, anyhow; not one has been reported as saved. In our cases the condition was deliberately allowed to subside and no attempt at operation was made. It was assumed that by the time the child was delivered the condition had advanced beyond the stage when operative cure could be expected. Both the children have atrophied testes, but they are alive and otherwise well, and their postnatal progress has not been marred by any surgical trauma or unwise attack.

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Reviews

CLINICAL MEDICINE

French's Index of Differential Diagnosis. Edited by Arthur H. Douthwaite, M.D., F.R.C.P. Seventh edition. (Pp. 1,058; 731 illustrations, 200 in colour. 105s.) Bristol: John Wright and Sons Ltd. 1954.

Handbook of Differential Diagnosis. By Harold Thomas Hyman, M.D. (Pp. 716. 55s.) Philadelphia, London, and Montreal: J. B. Lippincott Co. 1953.

Clinical Medicine: Some Principles of Thinking, Learning and Teaching. By R. D. Lawrence, M.A., M.D. Aberdeen, F.R.C.P. (Pp. 64+viii. 7s. 6d. paper bound.) London: H. K. Lewis and Co., Ltd. 1954.

Introduction à la Médecine: Principes, Idées Inspiratrices, Synthèses. By André Jacquelin. (Pp. 240. No price.) Paris: Librairie le François. 1954.

The seventh edition of French's *Index of Differential Diagnosis* is the most important of this group of books on differential diagnosis and the principles of medicine. It is essentially a guide to the practice of the art of medicine, and it is particularly concerned with the recognition of the phenomena of disease by the use of the unaided senses and with the depiction of the more bizarre effects of illness. It is 42 years since the first edition, and many of the older generation of consultants, who were brought up on "French," will look with interest, indeed almost with anxiety, to see how it has survived the passage of the years. Its external appearance is much the same; it has not become overweight or dropsical and contains only just over 1,000 pages. The list of contributors includes the names of a few eminent senior people, but for the most part they are young and in the middle ranks of the profession. The alphabetical arrangement of the text is as before, though the substance is almost completely changed to keep pace with modern advances. Here and there revision has not been ruthless enough, and the section on electrocardiography seems a bit behind the times, both in the use of standard leads and in the interpretation of fibrillation and flutter.

The illustrations have always constituted a major part of the appeal of this book. The best of the old are retained, and there are some good new black and white ones. There is a fine series on arthritis, including a memorable picture of Charcot's disease. In addition there are a number of coloured pictures, subjects such as the blood, the retina, and sigmoidoscopy being well illustrated in this way. The index is the key feature of a book of this kind; in the present instance it is full and effective, and the small print is remarkably clear. Dr. Douthwaite and his collaborators are to be congratulated on this new edition, which seems likely to please the present generation of students as much as the past, and to reach an honoured jubilee.

Dr. Hyman's *Handbook of Differential Diagnosis* is a much smaller book which is meant for the desk or the pocket. It is deliberately written in telegraphic style, and Dr. Hyman appears to have a collector's passion for lists. There is a 100-page list of occupational hazards and their diagnosis. There is a list of over a score of phobias, including phobophobia, the fear of fears; this is presumably the peculiar American malady which is appropriately treated by presidential wireless talks. There is a quite remarkable list of disturbances of sexual conduct. In fact this book recalls G. K. Chesterton's description of Macaulay's poem on the Armada as a geography book gone mad. Dr. Hyman seems to have a similar delight in the mere names of signs or symptoms. He communicates this to the reader, and the book has a curious quality of readableness. It will probably be of little value as a working manual, but it is a suitable book to keep in the car or some other place where there may be an odd moment to spare.

With Dr. Lawrence's *Clinical Medicine* we move from the collection of facts to the principles of thinking, learning, and teaching. Dr. Lawrence has written an essay on the problems of medical education, and he describes the methods he has himself used to organize his reading and experience, so as to remember things and be able to apply his knowledge in practice. He stresses the importance of interest and emotion in learning, and wisely recommends the student to read around his cases. He believes that the premedical subjects should be taught at the university and that the school years should be devoted to acquiring a good general education. He advises a considerable reduction in the amount of anatomy the student should have to learn, and the joint teaching of anatomy and physiology. The student should be introduced to the bedside as early as possible, and the general practitioner should play his part in medical education. Finally, he suggests that week-end conferences might be used for the instruction of junior teachers.

Dr. Jacquelin's *Introduction to Medicine* has the subtitle "Principles, Inspirational Ideas, Syntheses." It is described as a synthesis of the present and the past, and also a synthesis of the aetiology of diseases so that they may be regrouped in orders and hierarchies. Certain subjects lend themselves well to this treatment, such as the constitutional basis of disease, the adaptation syndrome of Selye, the conception of the collagen diseases, the psychosomatic attitude to disease which is popular in the West, and the cortico-somatic theory of Pavlov which is popular in the East. Dr. Jacquelin's style of writing is the antithesis of that of Dr. Hyman, being full and flowery. Of the medical consultation he writes:

> "Habit, which makes all things insipid and colourless, the repetition of a rite become mechanical, an automatism which develops little by little and ends in a sort of distraction, a gradual blunting of sensibility, not to say somnolence—there are so many psychological ways to degrade and, in a certain measure, to profane what ought to be held sacred."

Dr. Jacquelin's book will appeal to doctors of a philosophical turn of mind. When I lecture to my own students on these lines they ostentatiously close their notebooks and put on the glazed expression of someone waiting for a train which he knows cannot come for half or three-quarters of an hour.

L. J. WITTS.

HOSPITAL CARE AND AFTER

Hospital and Community. By T. Ferguson, F.R.S.Ed., D.Sc., M.D., D.P.H., F.R.F.P.S.Glas., F.R.C.P.Ed., and A. N. MacPhail, M.D., D.P.H. (Pp. 157. 9s. 6d.) Published for the Nuffield Provincial Hospitals Trust, London, New York, and Toronto: Geoffrey Cumberlege (Oxford University Press). 1954.

The Nuffield Provincial Hospitals Trust published in 1948 and 1950 the results of hospital community studies in Stirlingshire and Ayrshire, dealing with the availability and use of hospital services. The authors of this new study in Scotland, with the same title, report the results of observations in 1950–1 of the history and condition of 705 unselected male patients in acute medical wards in general hospitals in or near the City of Glasgow who were discharged after treatment. The effects of the impact of environment on the patient in relation to home and work were investigated and estimated three months after discharge and again 21 months later.

The statistical analysis of these results is detailed and impressive. Even more remarkable is the evidence of the social and economic circumstances of the patients included in the survey. Part of the field work was carried out by hospital almoners, and their investigations and advice were clearly of great value in assisting the physicians and the authors in finding or suggesting suitable jobs or in securing the adjustment of conditions of former employment to meet the needs of the patients discharged. Resettlement or rehabilitation was achieved in a considerable number of cases.

It would have been interesting to know to what extent the local health authority services were used in relation to after-care and in particular to have an account of how much collaboration was sought and obtained from the health visitors—for example, the Green Ladies (green by costume),

as they are popularly known, of Glasgow. In hospital and field research of this kind, and important research it certainly was, it is necessary to choose the staff best equipped by knowledge and experience; the capacity for good teamwork is of prime importance. But social research perhaps could be extended to include a practical demonstration of the possibility—or maybe the impossibility—of using statutory services in collaboration with clinicians, medical sociologists, and hospital almoners. The authors rightly emphasize that hospital care is merely an episode in the life of a patient, an incident dividing the past, in which the patient became ill, and the future, when he will return to his old ways and again need hospital treatment; or when he will change his habits and possibly his job and so maintain a satisfactory level of health; or make such changes as he can and put up with intractable factors of his environment, and so credit or debit his health account, as the case may be.

Professor Ferguson and Dr. MacPhail are to be congratulated on this zealous and detailed account of their investigations and findings. They have earned the gratitude of all workers in medical and social science, if only—and there is much more than this—for drawing attention to a valuable method of linking hospital care with after-care.

C. METCALFE BROWN.

PELVIC ANATOMY

Problems in the Anatomy of the Pelvis. By Eduard Uhlenhuth, Ph.D., with the assistance of DeWitt T. Hunter, M.D. (Pp. 206; 82 illustrations. 80s.) London, Philadelphia, and Montreal: J. B. Lippincott Co. 1953.

The authors of this volume do not pretend that it gives a complete account of the anatomy of the pelvis. The book has been written as a guide for a selected group of postgraduates and consultants who are especially interested in the specialized aspects of pelvic anatomy.

The subject-matter of the book is presented in three parts. Part I gives an extensive and accurate account of the extent and relationships of the retrovesical space. The authors stress the importance of this space from the surgical aspect, and point out that none of the pelvic organs is excluded from it. Parts II and III contain descriptions of the bladder musculature and the muscles of the pelvic diaphragm. A detailed account is given of the arrangement of the musculature of the bladder and its sphincters from the embryological, histological, anatomical, and physiological aspects. There is a comprehensive atlas of the dissections on which the descriptive part of the book is based. The illustrations are well executed and reproduced. This book can be recommended to surgeons, gynaecologists, and others interested in pelvic anatomy.

W. J. HAMILTON.

ATLAS OF BLADDER NECK

Atlas of the Urethral Aspects of Diseases of the Prostate and the Bladder Neck Showing Urinary Obstruction. By Dr. Kurt Tzschirntsch. (Pp. 159; illustrated. 110 Dutch guilders.) Leyden, Holland: L. Stafleu. 1953.

In spite of the fact that perurethral resection of the bladder neck is a long-established surgical procedure, no comprehensive atlas of the posterior urethra or bladder neck comparable with those atlases of the cystoscopic appearances of the bladder has been published before. This book is an excellent atlas of the bladder neck and prostatic urethra as affected by various lesions of the prostate gland. The author takes separately the various appearances of the five main lesions by which the bladder neck is affected—benign hypertrophy of the prostate gland, carcinoma of the prostate, sclerosis of the internal sphincter, resection of obstructive tissue and strictures, and diverticula and other anomalies. These are depicted as seen through a resectoscope. The special importance of this work is the fact that all the urethroscopic pictures have been painted by the author himself, who is a most accomplished artist, so that here are shown beautiful illustrations of the most important endoscopic appearances, in the fullest detail and in the true colouring, by one who is constantly examining the urethra and knows the pathology of the structures he is studying. Such circumstances can never be attained by the professional artist, to whom each structure and detail must be indicated and described and then may so easily be confused by changes of illumination and irrigation; moreover, it is almost impossible to keep the examining instrument immobilized for him during the painting.

The 30 paintings of the bladder neck showing how it may be affected by benign enlargement of the prostate have been so well chosen as to be almost a perfect pictorial demonstration for endoscopic resection. The illustrations of the endoscopic appearances of carcinoma of the prostate show most effectively just those changes in appearance which distinguish the malignant from the benign gland. The only criticism which might be made is that it is a pity the author has confined himself to depicting causes of obstruction of the bladder neck or those seen in the course of endoscopic resection. We may hope that in a future edition this atlas will be enlarged to depict all the lesions of the posterior urethra, in the female as well as in the male.

An excellent translation in English both of the description of the cases as well as that of the individual illustrations is given on the lower half of each page, and the author acknowledges Mr. R. Lester Williams's part in the supervision of the translation. This atlas is primarily designed to show the beginner what he sees through a resectoscope and what he should look for, but it will prove as interesting as it will be instructive to the experienced urologist, and it will also be a standard of excellence for urethroscopic illustrations.

J. E. SEMPLE.

ACUTE OEDEMA OF THE LUNG

Acute Pulmonary Edema. By Mark D. Altschule, M.D. Modern Medical Monographs 10. (Pp. 68. $3.50.) New York: Grune and Stratton. 1954.

The problem of the pathogenesis of acute pulmonary oedema is still far from solution. The rapid onset, the desperate character of the attack, and the grave danger in which the patient is make it very difficult to obtain any real understanding of what goes wrong. In this little monograph one finds an interesting and sensible review of the whole question, though the author will be the first to admit that much remains to be discovered and that treatment is often very unsatisfactory. It is curious that oedema of the lungs does not occur more readily when one recalls that the pressure in the pulmonary bed is quite often much higher than the osmotic pressure. No doubt here the state of the vessel walls is very important. The author emphasizes the importance of lymphatic drainage in the lungs, which must play a part in getting rid of accumulation of fluid.

Dr. Altschule divides the attack into five phases: the onset, the interstitial phase (this presumably presents the remarkable shadow at the roots of the lungs), the intra-alveolar phase, the phase of shock, and the terminal phase. How far shock is the result of the failure of the circulation in the lungs or the result of its cause seems to be difficult to decide. One of the unexpected causes of acute pulmonary oedema is damage to the brain. The author thinks that aortic stenosis is less frequently associated with acute oedema of the lungs than is aortic incompetence; that in mitral stenosis it is the increase in the rate of the heart, with consequent shortening of diastole, which is the important feature—he does not mention the occurrence of this when fluid has been aspirated too quickly from the chest. Experimental work still fails to produce a simple explanation of pulmonary oedema. No doubt there is a combination of causes in diseased persons. Morphine is still the drug of choice, but aminophyllin is said to be useful given intravenously. Venesection also has a definite place in treatment.

There is a full list of references. The book is written in a clear and interesting manner. Though perhaps but little addition is made to the reader's knowledge, it is interesting to peruse such a well-balanced and clear survey of existing information.

TERENCE EAST.

BRITISH MEDICAL JOURNAL
LONDON
SATURDAY JULY 10 1954

THE PRESIDENTIAL ADDRESS

By joining physicians and surgeons in one Faculty—the Faculty of Physicians and Surgeons—at the end of the sixteenth century Maister Peter Lowe took a step which is thought by the historian of Scottish medicine—an Edinburgh man—to account for the traditional all-round excellence of Glasgow medical graduates as general practitioners. It was therefore more than appropriate that the President, Sir John McNee, should choose as the theme of his address at the Annual Meeting of the Association at Glasgow this week "The Practice of Medicine." Sir John McNee approached his theme on a note which is being sounded to-day in many parts of the world, as was evident at the first World Conference on Medical Education held by the World Medical Association in London in August last year. His is a theme, for example, about which more and more is being heard in the United States of America, a country where technical methods combined with intense specialism have tended to replace the classical observational approach of the doctor to the practice of medicine. The same tendency is visible in Britain. The modern student may be led to believe that the *x*-ray film is the principal or even the sole diagnostic weapon in diseases of the lung, the electrocardiogram in diseases of the heart, and so on. And he may be encouraged to think along these lines by those teachers who specialize in such subjects and to whom the technical refinements now at their disposal are all-important in research. Sir John McNee, looking back to get the present in true perspective, reminds us that the President of the first Annual Meeting of the B.M.A. in Glasgow, Sir William Tennant Gairdner, in 1888 chose as the theme of his presidential address "On the Physician as Naturalist." The subsequent shift of emphasis in Medicine was shown in the presidential address at the second meeting in Glasgow in 1922, when Sir William Macewen, who as a student had been a dresser in Lister's wards in the Royal Infirmary, spoke on the surgery of the brain. The development of specialism has led to remarkable advances in the diagnosis and treatment of disease, indeed to a more precise knowledge of how the body works. But "the practice of medicine" is the principal professional activity of the majority of doctors. In what framework of thought should this practice be conducted?

Sir John McNee, asking the question whether the physician needs to study the natural history of diseases so closely as before, considers that he does. His long experience as a teacher has convinced him that a complete and accurate diagnosis can frequently be made "by using the simple observational methods of the trained naturalist." Such a statement from a man who has been research worker as well as teacher comes at a highly opportune time—at a time when specialism is being vigorously pursued, with its inevitable stress on special investigations. Important as such work is, it nevertheless carries with it some dangers. First, it leads to the belief that the observational approach of the trained naturalist has exhausted itself as an instrument of medical research and that advance will come only through the laboratory. Yet it is not so long ago that Dr. William Pickles, of Aysgarth, made his important contributions to epidemiology by the apparently simple methods of observation in the course of a busy general practice. Sir John McNee also instances the work of Sir Norman McAlister Gregg, in Australia, on the relationship between maternal rubella and congenital defect. Secondly, the student, taught in a hospital manned largely by specialists, may be tempted to lean too heavily on the resources of the *x*-ray and pathological departments in the diagnosis of disease and to rely less and less on the diagnostic potentialities of his senses, aided by simple instruments which can be used at the bedside. "Further investigations . . . constitute," as Sir John puts it, "the great and fundamental difference between Medicine in Gairdner's day and in our own." And he pleads cogently for a correct order of approach and appraisement: first the clinical history, then "close search for symptoms and signs of disease," and lastly the "further investigations." In the practice of medicine the majority of doctors have to apply their art and science, often as a matter of urgency, away from the well-ordered mechanism of a hospital and its numerous special departments. They have to rely first and foremost on their own senses, with such extensions of them as can be carried in a bag.

Is there a risk that to-day the medical student in the hospital is not thoroughly grounded in the observational approach? Sir John seems to hint that the risk is there. "The professor or clinical teacher," he states, "whose range as a teacher embraced most of medicine or of surgery, is gradually becoming extinct; and we must think carefully how to fit in specialists as professors and clinical teachers while still retaining

a correct balance in the training. . . . A broad view is required, and specialism is perhaps not the best way in which to acquire it." This is one of the most important problems of medical education—how to teach the student the broad view so that he may be fitted to carry on the practice of medicine, how to teach him this in a hospital staffed largely by men intensively engaged in the pursuit of specialist studies. One way of putting the "broad view" before the student is to bring the general practitioner into the teaching team, a movement already on foot. Sir John McNee's apposite words seem to express a wish for the re-emergence of the general physician, now becoming almost extinct in a world of specialists. He touches upon many other aspects of the practice of medicine in his thoughtful and valuable presidential address, printed in our opening pages this week; but running through it is a plea for a holistic approach to the practice of medicine and, to achieve this, for a similar approach to the teaching of the Art, firmly based, as it must be, upon the Sciences that provide its foundation.

PREVENTION OF POLIOMYELITIS

One gramme of faeces from a poliomyelitis patient may contain enough virus to infect one million monkeys.[1] Every poliomyelitis patient excretes virus in his faeces for the first ten to fourteen days of his illness. Half the patients are still excreting virus in their faeces after three weeks, and a quarter after five to six weeks; a few continue to excrete virus for as long as twelve weeks. In addition, every patient has virus in his pharynx for three to five days before the onset of the acute stage and for three to seven days after.[1] There need be no doubt about the infectivity of the acute case.

Virus enters the body by the mouth, and family life makes easy the hand-to-mouth transfer of virus from either the pharynx or faeces of the patient to the alimentary tract of other members of the household. These infect their playmates or workmates outside, and in a short time infection from one case may spread widely. In an extensive epidemic infection may thus appear to be indiscriminate, but virological studies indicate that virus is found mainly in the intimate associates of the paralysed patient.[1] Few of the contacts become ill, and, when they do, the symptoms of the "minor illness" may be very unlike paralytic poliomyelitis. In spite of this difficulty, it is often possible by careful inquiry to trace the spread of infection, from case to contact and from contact to case, in an outbreak with no apparent pattern. Many such reports have been published and these have been reviewed already in this *Journal*.[2] Can anything be done to stop the spread of infection? The most elementary step is to isolate the patient. But hospitalization and isolation are not synonymous, and it is unfortunately true that children have been infected while in hospital. Banks[3] reports a series of 55 paralytic patients of whom no fewer than 12 were apparently infected in children's wards or nurseries, and Ferguson[4] reports another two cases. It is not justifiable to nurse cases of poliomyelitis in open general wards. They should be admitted either to cubicles or to wards dealing only with poliomyelitis, and, so far as possible, they should be treated by nurses who are not handling other children. The usual measures for individual and collective protection against infection must be applied.[5]

It has been known for some time that prophylactic inoculations against diphtheria or whooping-cough may precipitate paralysis in a patient infected with poliomyelitis virus, and it is becoming apparent that any form of injection treatment may have this effect. Banks[3] reported that six of the ten paralysed young children had had penicillin injections in the buttocks or thighs and in all of them the paralysis was confined to the lower limbs; the other four children had not had penicillin injections and none of them had paralysis of the legs. Ferguson[4] and Logan[6] report other examples. In this connexion the work of Trueta and Hodes[7] is of great interest: working with mice, they showed that "widely different types of stimuli—plaster casts, exercise and peripherally injected irritants—produce macroscopic changes in the circulatory patterns of the spinal cord," and they suggest that "many of the factors that enhance the severity of poliomyelitis, or localize the paralysis, may operate through local vascular changes in the brain and spinal cord. . . . Of the potential damaging influences commonly used in medicine, among the most potent are (1) spinal puncture and (2) the injection of various substances." It is obvious, on both clinical and experimental grounds, that injections to children during poliomyelitis epidemics should be reduced to a minimum. Oral penicillin usually gives satisfactory serum levels.

[1] *Wld Hlth Org. techn. Rep. Ser. No. 81. Expert Committee on Poliomyelitis, First Report*, 1954.
[2] *British Medical Journal*, 1953, 11, 1258.
[3] *Lancet*, 1954, 1, 464.
[4] Ibid., 1954, 1, 682.
[5] *Hospitalization of Patients suffering from Poliomyelitis in its acute stage. European Association Against Poliomyelitis, 2nd Symposium*, 1954.
[6] *Lancet*, 1954, 1, 734.
[7] Ibid., 1954, 1, 998.
[8] Agerholm, M., ibid., 1953, 11, 287.
[9] *Report on the Work of the Public Health Department, County Borough of Southend-on-Sea*, 1952.
[10] *J. Amer. med. Ass.*, 1952, 150, 757.
[11] *Gamma Globulin in the Prophylaxis of Poliomyelitis*. U.S. Department of Health, Public Health Monograph No. 20. 1954.
[12] *J. Amer. med. Ass.*, 1953, 154, 1086.
[13] *Amer. J. med. Sci.*, 1953, 226, 125.
[14] *Proc. roy. Soc. Med.*, 1953, 46, 997.

When the patient goes to hospital he leaves a great deal of virus in the home. Most members of the family are infected at the same time as the patient, although less than 10% of infected families have more than one paralytic case.[1] For their own protection, injections and violent exercise should be avoided for two to three weeks and any illness however trivial should be treated by rest in bed. They should be given careful instructions in hygiene to prevent spread by faecal contamination. Visitors to the house and visits to other houses should be discouraged, but there is a growing tendency to advise stricter quarantine measures.[8] The main difficulty in applying such measures is the impossibility of detecting infected persons. The development of tissue culture technique may largely remove this difficulty. An experimental quarantine scheme, with Taunton Borough and Taunton Rural District functioning as a combined area for the purpose, with a population of approximately sixty thousand, will be in operation this summer. It is intended to regard as intimate contacts those who have been living in the same house and those who have been using the same domestic lavatory. Where conditions are suitable, contacts will be confined to their own house and garden for three weeks. Health visitors and others will help with shopping, and some financial help will be available to make up for loss of wages. Quarantine will be on a voluntary basis. This is a scheme of great interest and may yield answers to many doubts. Logan[9] states that "the probable advantages to be derived from administrative measures have to be weighed against the inconvenience and loss which they will occasion, and when adopted they cannot be pushed to anything like a logical conclusion without grave dislocation of our daily life." This is common sense, but it must be admitted that the logical conclusion of our present policy is uncontrolled spread of infection.

The work of Hammon and his colleagues[10] on gamma globulin seemed to show in well-controlled experiments involving over 54,000 children that, from the second to the sixth weeks after injection of gamma globulin, there was protection against paralysis: during the first week after injection there was no protection but possibly some modification of the disease. In 1953 a trial of gamma globulin on a national scale was carried out in the United States. The object was to assess the value of gamma globulin both for mass use in the general population and for contact use in the households of poliomyelitis patients. The report[11] and summary[12] show that, in the first group, almost 235,000 children were inoculated; in the second group there were 749 multiple-case households and 158 patients received gamma globulin before the onset of symptoms. There were no controls. In neither investigation was any significant effect of gamma globulin demonstrated. In a comment which follows the report Hammon agrees with these findings, but states that no dramatic effect could have been expected on experimental grounds: he claims that the report does not prove that gamma globulin did not have the effects which could have been scientifically predicted. This is fair comment, and it is fair also to state that Hammon[13] has previously emphasized the limitations in the use of gamma globulin in poliomyelitis. The difficulties of such widespread investigation are fully realized, but the results show clearly that gamma globulin cannot satisfy widespread demands for protection against poliomyelitis. Perhaps the most fruitful use of gamma globulin would be in the households not of the case but of the contacts. Where, for example, a case occurs in a day school, the contacts of that case carry the infection home to a virus-free household. Would not the use of gamma globulin in that household prevent paralytic cases in members of the family? Coupled possibly with some degree of quarantine, would it not, in some measure, prevent further spread of the disease in the community? A study of the outbreak analysed by Agerholm[8] and possibly also Logan's papers[9 14] may suggest that it certainly would. The findings of Hammon on the protective power of gamma globulin are not invalidated by the 1953 American report. But the necessity for intelligent use of this protection is firmly emphasized.

Active immunization against poliomyelitis may be a sounder policy. Tissue culture has made the preparation of vaccine practicable, and two types, one inactivated and one attenuated, are being investigated. "Experiments in animals, and a limited but significant number of tests in human volunteers, have shown that vaccines of such types consistently induce the formation of specific antibodies and, at least in the monkey, result in subsequent resistance to infection with a challenge virus." This is a hopeful statement, though the W.H.O. report[1] from which it is extracted insists that mass immunization should not be generally adopted until "the innocuity and efficacy of the vaccines and the level and duration of the immunity" have been sufficiently studied.

PROGNOSIS IN CANCER OF COLON AND RECTUM

The question whether surgery can appreciably improve the prognosis for patients with cancer—other than those who would not in any event succumb to their disease for many years—has been raised in a number of recent papers.[1-3] The thesis which has been put forward,

particularly in relation to cancer of the breast and cancer of the stomach, is that spread to distant organs takes place in many growths before the earliest signs or symptoms present themselves in such a way as to cause concern to the patient or his doctor. This has led to the suggestion that surgical treatment is likely to be of more than palliative value only with certain tumours of inherently slow rates of growth. If this were so, it would of necessity follow that increasing efficiency of diagnosis and of surgical technique could not improve the cure rate above a certain limiting value. Evidence that this may be true of cancer of the large bowel has now been put forward by Grinnell[4] from the records of the Presbyterian Hospital, New York.

Over the 30 years 1916 to 1945, 890 patients were admitted suffering from cancer of the colon and 777 from cancer of the rectum. For the whole period the five-year survival rates were respectively 27% and 26%. The rates, however, varied much within this period—increasing from 6% and 18% in 1916–20 to 32% and 33% in 1936–40, and falling slightly in the succeeding five years. Throughout the 30 years the proportion in which it was possible to attempt a curative resection rose steadily, and by the end of the period had reached two-thirds of the total. Subsequently, for cancer of the colon, it rose to three-quarters. When the cases in which a curative resection was undertaken are considered separately, the five-year survival rate is found to have been appreciably higher after 1930 than before, but there is no evidence of any real improvement subsequently. Much of the initial improvement can clearly be attributed to a reduction in operative mortality (from a figure of between 30 and 40% to approximately 6%); and when this is allowed for by expressing the number of five-year survivors as a percentage of those surviving operation rather than of all those coming to operation, it is seen that the end results for the period 1941–5 were slightly worse than those obtained in patients operated on 20 years earlier. The author's conclusion that treatment had become less effective is perhaps hardly justified, even though he can point to the retirement in 1940 of a surgeon whose operative skill in this field was outstanding. Allowance must certainly be made for the increasing average age of the patients operated on, and this alone would have a considerable effect on a crude five-year survival rate. Nevertheless the results underline the fact that, although improvements in surgical and anaesthetic technique and in post-operative care are steadily extending the proportion of growths which can be operated on, there is as yet no evidence of any similar improvement in the outlook for those patients in whom the primary tumour has been successfully removed.

Expressed as a percentage of patients surviving operation, the New York figures for five-year survivals are, as a whole, slightly better than those which have been recorded in Britain. For cancer of the rectum, for example, the figure for the Presbyterian Hospital for the whole period 1931–45 was 53%, whereas the corresponding figure for the United Birmingham Hospitals[5] was 48%, for St. Mark's Hospital[6] 46%, and for cases treated in all the London hospitals[7] in 1938–9 42%. These differences may conceivably be explained by differences in the type of case at the various hospitals—particularly by differences in age. It is, however, unlikely that the same can be said for the large differences recorded for the survival rate expressed as a percentage of the total number of patients coming for treatment. These vary from 29% at the Presbyterian Hospital between 1931 and 1945 to 12% at the United Birmingham Hospitals and in the London survey. Some of the advantage apparent in the American series may well be attributed to the greater proportion of patients in whom a cure was attempted.

[1] Park, W. W., and Lees, J. C., *Surg. Gynec. Obstet.*, 1951, **93**, 129.
[2] Kreyberg, L., *Brit. J. Cancer*, 1953, **7**, 157.
[3] Swynnerton, B. F., and Truelove, S. C., *British Medical Journal*, 1952, **1**, 287.
[4] *Surg. Gynec. Obstet.*, 1953, **96**, 31.
[5] *Annual Cancer Report of the United Birmingham Hospitals*, Vol. 1, 1953. Alimentary Tract.
[6] Gabriel, W. B., *Principles and Practice of Rectal Surgery*. 1948. London.
[7] Harnett, W. L., *Survey of Cancer in London*. 1952. British Empire Cancer Campaign, London.

FOETAL HEPATITIS

Hepatic disease in infancy is not common in Britain, but reaches serious proportions in other parts of the world, especially in the period after weaning. Most of such cases are attributed to severe protein deficiency in the diet or to the ingestion of hepato-toxic alkaloids in the vegetable infusions consumed instead of tea in the West Indies and elsewhere. Even in areas where these factors are unlikely to operate, cases of infantile cirrhosis do occur, and their aetiology remains a baffling problem. Some are undoubtedly due to congenital obliteration of the bile ducts or to syphilis acquired *in utero*. Some authorities regard erythroblastosis foetalis as causative, although the evidence for this is unconvincing. Infective hepatitis, which apart from alcoholism is probably the commonest cause of cirrhosis in non-tropical countries, has not been regarded in the past as likely to be responsible for cirrhosis in infancy owing to the long incubation period of both forms of the disease and the relatively long intervals between the acute phase and the development of cirrhosis. The recognition, therefore, by Dible and his colleagues[1] that hepatitis may occur in the foetus sheds a new light on the aetiology of infantile cirrhosis.

Six cases were studied by these authors; four, in which the babies died within the first two days of birth, were in an acute or necrotic phase, and two, in which the babies lived respectively for three and seven weeks, were in a subacute or cirrhotic phase. The histological changes in the acute phase included extensive necrosis of parenchymal cells, bile-duct proliferation, areas of liver cell regeneration, and conspicuous haemopoietic foci. Histiocytic reaction and a fine pericellular type of fibrosis were prominent. Other noteworthy features in all four cases were the presence of many multinuclear giant cells, apparently derived from the parenchymal cells, and granules of iron-containing pigment in liver and histiocytic cells. The advanced stage of these various

[1] *J. Path. Bact.*, 1954, **67**, 195.
[2] Cappell, D. F., and McFarlane, M. N., ibid., 1947, **59**, 385.
[3] France, N. E., and Wilmers, M. J., *Lancet*, 1953, **1**, 1181.

changes is, as emphasized by the authors, only compatible with a disease process that has arisen some considerable time before birth. What is perhaps less obvious is the identification of the lesions with those of infective hepatitis. The presence of conspicuous foci of haemopoiesis and the Prussian-blue reacting pigment, features not seen as a rule in infective hepatitis in adults, undoubtedly favour the diagnosis of erythroblastosis foetalis, which is already regarded by many as a cause of liver damage in the newborn. No evidence of maternal antibodies to the infant's red cells could, however, be demonstrated in any of the six cases, despite careful and expert search. Moreover, although histologically iron appeared to be present in excess, chemical analysis showed that the quantity present was within normal limits. Finally, haemopoiesis is a normal function of the liver up to the time of birth, and the persistence of this function slightly beyond its normal time is common in other forms of neonatal hepatic disease. Erythroblastosis may therefore be regarded as certainly excluded, and, when allowance is made for such features as may be attributed to the special age and reactivity of the liver, the pathological picture is of an infective hepatitis that has undoubtedly arisen *in utero*. Whether the causative agent is identical with either of the viruses responsible for hepatitis in adults, or whether some other virus is responsible, will be decided only by adequate transmission experiments with material from future cases. That hepatic necrosis in the foetus can occur in cytomegalic inclusion disease[2] and as a result of infection with herpes virus[3] has already been recorded.

The greater severity of the disease in the left lobes is noted by Dible *et al.* in two of their four acute cases. Such a difference in adults has been attributed to the right lobe of the liver obtaining a better supply of protective factors from the alimentary canal. In the foetus it is probably due to the early atrophy of the right umbilical vein, so that any infective agent passing the placenta later in pregnancy travels via the left umbilical vein and falls primarily on the left hepatic lobe.

DRUG TREATMENT OF ANGINA

Glyceryl trinitrate is well established as a drug which relieves pain during the actual attack of angina pectoris, and unpleasant symptoms resulting from peripheral vasodilatation are less frequent and less severe with it than with amyl nitrite. On the other hand, methods of treatment intended to improve coronary flow and prevent attacks have not given consistent results, initial favourable reports seldom having been substantiated. Conflict of evidence may arise from difficulties in interpreting results, and Silber and Katz[1] have recently analysed some of the possible errors in clinical investigations of drugs used in angina pectoris.

Aminophylline was found by Master and his colleagues[2] to be the best of fifteen drugs investigated for their prophylactic effect. Even then, the results achieved were no better than with a placebo. Moreover, Foltz and his colleagues[3] were unable to demonstrate any significant change in coronary flow in the dog after giving aminophylline. Evans and Hoyle[4] considered papaverine to be of doubtful value only; and Katz,[5] after first reporting favourably on the effect of large doses (400–500 mg.) of this drug, subsequently[6] agreed that its value was limited. Similarly unconvincing results have been reported with ethaverine[7] (the ethyl analogue of papaverine), vitamin E (alpha tocopherol),[8 9] mannitol hexanitrate,[4] and erythrol tetranitrate.[4] Pentaerythritol tetranitrate, used originally by Bjĕrlov,[10] has been regarded favourably by some authors[11 12] and less so by others.[13 14] The usefulness of khellin[15] is limited by the gastric disturbance which it often provokes: this is said to be less severe with pure crystalline preparations.[16] Vomiting is not due solely to local irritation, since it occurs also after intramuscular injection. Khellin suppositories[17] have been suggested as the most suitable mode of administration, but the evidence for this is weak.

The work of Gofman and his co-workers[18] on the relationship between size of blood lipoid molecules and atheroma has influenced investigators to search for methods of inhibiting atherogenesis. Restriction of dietary fat, however, unless severe, has no influence on this molecular pattern. Heparin has been shown[19] to lower the concentration of the moderate-sized lipo-protein molecules and, if given once or twice weekly, to diminish the frequency of anginal attacks: but these findings have not been confirmed by others.[20 21] The rarity of this disease in women of child-bearing age has led to the use of oestrogens, with some favourable results.[22 23] Pick[24] showed that experimental coronary atherosclerosis could be reversed by oestrogen; and Oliver and Boyd[25] have reported reduction of hypercholesterolaemia in man (without, however, effecting any improvement in effort tolerance). This line of research, which is still in progress, may provide information about the prophylaxis and therapy of angina. Meanwhile the importance of general measures to reduce the work of the heart must not be overlooked: this applies particularly to weight reduction in the obese and to the correction of anaemia.

[1] *J. Amer. med. Ass.*, 1953, **153**, 1075.
[2] *Amer. J. med. Sci.*, 1939, **197**, 774.
[3] *Circulation (N.Y.)*, 1950, **2**, 215.
[4] *Quart. J. Med.*, 1933, **2**, 311.
[5] *J. Amer. med. Ass.*, 1942, **120**, 434.
[6] Simon, A. J., Dolgin, M., Solway, A. J. L., Hirschmann, J., and Katz, L. N., *J. Lab. clin. Med.*, 1949, **34**, 992.
[7] Degenhardt, D.P., and Hodgkinson, R., *Brit. Heart J.*, 1954, **16**, 142.
[8] Vogelsang, A., and Shute, E. V., *Nature (Lond.)*, 1946, **157**, 772.
[9] Makinson, D. H., Oleesky, S., and Stone, R. V., *Lancet*, 1948, **1**, 102.
[10] *Svenska LäkT.*, 1943, **40**, 694.
[11] Winsor, T., and Humphreys, P., *Angiology*, 1952, **3**, 1.
[12] Plotz, M., *N.Y. St. J. Med.*, 1952, **52**, 2012.
[13] Talley, R. W., Beard, O. W., and Doherty, J. E., *Amer. Heart J.*, 1952, **44**, 866.
[14] Weitzman, D., *British Medical Journal*, 1953, **2**, 1409.
[15] Anrep, G. V., Barsoum, G. S., Kenawy, M. R., and Misrahy, G., *Brit. Heart J.*, 1946, **8**, 171.
[16] Best, M. M., *Amer. J. med. Sci.*, 1952, **224**, 308.
[17] Kenawy, M. R., Barsoum, G. S., and Bagouri, M. M., *Eye, Ear, Nose Thr. Monthly*, 1950, **29**, 79.
[18] *Circulation (N.Y.)*, 1950, **2**, 161.
[19] Graham, D. M., Lyon, T. P., Gofman, J. W., Jones, H. B., Yankley, A., Simonton, J., and White, S., ibid., 1951, **4**, 666.
[20] Gruner, A., Hilden, T., Raaschou, F., and Vogelius, H., *Amer. J. Med.*, 1953, **14**, 433.
[21] Rinzler, S. H., Travell, J., Bakst, H., Benjamin, Z. H., Rosenthal, R. L., Rosenfeld, S., and Hirsch, B. B., ibid., 1953, **14**, 438.
[22] Bonnell, R. W., Pritchett, C. P., and Rardin, T. E., *Ohio St. med. J.*, 1941, **37**, 554.
[23] Lesser, M. A., *New Engl. J. Med.*, 1942, **226**, 51.
[24] *Circulation (N.Y.)*, 1952, **6**, 858.
[25] *Proceedings of the British Cardiac Society*, reported in *Brit. Heart J.*, 1954, **16**, 124.

BRITISH ASSOCIATION OF PAEDIATRIC SURGEONS

The inaugural meeting of the British Association of Paediatric Surgeons was held at the Hospital for Sick Children, Great Ormond Street, and the Royal College of Surgeons, on June 30 and July 1 and 2. During the meeting there were discussions, clinical demonstrations, films of surgical procedures, operative demonstrations, and an exhibition illustrating a wide range of problems in children's surgery.

In welcoming the 110 delegates, including many from abroad, the President (Mr. DENIS BROWNE) said that paediatric surgery was a rapidly developing part of medical practice and it was the aim of the Association, not to try to develop a monopoly, but to set a standard in the surgical care of children.

"Imperforate Anus," Intussusception, and Congenital Megacolon

Opening a discussion on congenital malformations of the rectum and anus, Mr. Denis Browne (London) emphasized the importance of a close inspection of the perineum in order to distinguish between cases in which an anus was present but stenosed, ectopic, or covered by skin, and those in which the anus was absent. In the former group a sphincteric muscular ring was present and it was necessary to preserve it. He had seen many cases of ectopic anus in which attempts to create an opening into the rectum from the perineum had had disastrous results. The position was aggravated by the grouping of all these conditions under the term "imperforate anus" and he thought much bad treatment in this region was due to misleading terminology.

Mr. R. B. ZACHARY (Sheffield) opened a discussion on acute intussusception in childhood. He first considered management of the gangrenous intussusception and stressed the importance of adequate pre-operative resuscitation. He then described conservative treatment by means of the hydrostatic effect of a barium enema, and his experiences in a series of 54 cases. With selection, success could be achieved in a high proportion of cases, but experience and an awareness of the dangers were necessary.

Dr. ORVAR SWENSON (Boston) delivered the Simpson-Smith Memorial Lecture of the Institute of Child Health on congenital defects in the pelvic parasympathetic nervous system. He described how the investigation of 12 children with congenital megacolon had shown that the terminal narrow segment failed to conduct peristalsis and how, after resection, it was found to lack ganglion cells. The operation of recto-sigmoidectomy was described and the technique he employed now. He spoke next of investigations which led to the conclusion that in certain cases of megaloureter there was an almost complete absence of ganglion cells in the bladder wall. Partial cystectomy with wide resection of the bladder neck had been successful in some of these cases, but he stressed the importance of bladder training and frequent re-examination after operation.

Vomiting in Infancy

An important cause of persistent vomiting in infancy, incompetence of the cardia, was dealt with by Miss ISABELLA FORSHALL (Liverpool) in a paper on "The Cardio-oesophageal Syndrome in Childhood." Two conditions were involved, she said: that of lax oesophagus with the cardia below the diaphragm, and hiatus hernia in which it lay above. In the former, vomiting often dated from birth and, in nearly half the cases, was projectile. Recumbency aggravated the condition and so the infants should be nursed in the upright position and the feeds thickened. Operation was rarely required. With sliding hiatus hernia, on the other hand, reflux oesophagitis was common and the symptoms were more severe. Secondary shortening and stricture of the oesophagus were real dangers and she thought operative repair of the hernia was always necessary.

Mr. DAVID WATERSTON (London) emphasized the need for close co-operation between physician and surgeon in the treatment of this difficult condition. He described his concept of hiatus hernia as a congenital lesion of the oesophageal opening of the diaphragm and his views of the relevant surgical anatomy. He advised operation for children with stricture or severe oesophagitis and for a few infants in the first year of life whose development was severely retarded. During the discussion which followed Mr. R. H. R. BELSEY (Bristol) pointed out the rapidity with which stricture formation could occur and the necessity for oesophagoscopy whenever oesophagitis was suspected. He had had to perform resection in 20 cases with advanced strictures.

Intestinal Obstruction

On the final day Mr. H. H. NIXON (London) read a paper on intestinal obstruction in the neonatal period. Of the classical triad—constipation, abdominal distension, and vomiting—the former two were sometimes difficult to evaluate: meconium could be passed in the presence of an obstruction and the abdomen of the newborn infant was naturally protuberant. Vomiting was therefore the most reliable early symptom, and he thought delay in diagnosis, which still occurred commonly, was largely owing to failure to appreciate the importance of bile-stained vomiting during the first days of life. Mr. Nixon described investigations he had carried out into the aetiology and treatment of ileal atresia, and suggested that resection of the atretic segment together with the dilated loop of bowel above it and end-to-back anastomosis was the treatment of choice.

Mr. P. P. RICKHAM (Liverpool), discussing peritonitis in the neonatal period, said there were two forms to consider—bacterial peritonitis and that due to the presence of meconium in the peritoneal cavity—and they were not as rare as was often believed. Most forms of intestinal obstruction in the newborn were complicated at times by meconium peritonitis, though the perforation of the bowel which had occurred *in utero* often had closed before birth and was not evident at operation. This complication adversely affected the prognosis, but cases had been operated upon successfully. The treatment of bacterial peritonitis was that of the primary condition, which in some cases was a blood-borne infection. In the ensuing discussion Mr. DENIS BROWNE warned of the need to make sure, before operation, that there was not a plug of inspissated meconium or mucus in the rectum causing the obstruction.

Dr. T. EHRENPREIS (Stockholm), speaking as a guest lecturer of the Institute of Child Health, described the clinical and radiological features of Hirschsprung's disease in the neonatal period and showed a film of the operation of rectosigmoidectomy.

A most successful meeting concluded on Friday evening with a dinner in the Apothecaries' Hall (see p. 107).

BRITISH EMPIRE CANCER CAMPAIGN

The annual general meeting of the British Empire Cancer Campaign was held at the House of Lords on June 29, the DUKE OF GLOUCESTER presiding. His Royal Highness referred with regret to the death of Professor F. L. Hopwood, honorary secretary of the Campaign, and one of those who helped to found it in 1923. "Hopwood," he said, "was one of the men who inspired admiration and affection, and he has well deserved our thanks." The Duke added that the demands on the Campaign were increasing; the annual expenditure on research had trebled since the war and had kept pace with the reconstruction of laboratories, training of personnel, and production of up-to-date equipment which combined to make the intensification of cancer research possible.

LORD HORDER, in proposing a vote of thanks to the Duke, referred to the new outlook on cancer. The old shibboleths were passing away and were being replaced by a more common-sense and rational outlook towards the subject. He also referred to the forthcoming Sixth International Congress in Brazil, at which the delegates from the Campaign

would be Sir Stanford Cade, Professor Windeyer, and himself, with Captain Tours (secretary). These international congresses were of inestimable value.

On the proposition of Dr. CUTHBERT DUKES, seconded by Professor D. W. SMITHERS, Professor R. W. SCARFF was elected honorary secretary in succession to Professor Hopwood.

The Campaign's Research Programme

Professor F. DICKENS, in presenting the annual report, said that the report embodied the principal results of the researches of no fewer than 29 independent research centres, each a team of from a few workers to more than 60 at the largest centre, as well as those of 26 individuals in charge of research grants and 15 holders of research fellowships. On the question of tobacco smoking and cancer of the lung the Campaign was actively promoting investigations. No conclusive results were yet available as to the presence of any known carcinogen in tobacco smoke, though it seemed that there was none of an activity comparable with coal tar. So far no suitable method had been devised for inducing lung cancer in animals. In spite of the urgency of this problem, the experimental work was, from its nature, bound to take many months.

Research into methods of treatment of cancer, Professor Dickens went on, was proceeding hand in hand with those on causation. Surgery and radiation remained the accepted treatments for most cancers, and in the field of radiotherapy the opening of the new cobalt-60 beam therapy unit, the generous gift to the Campaign of a Canadian benefactor, Mr. J. W. McConnell, had now made available for research the very intense gamma rays produced by that source.

After a reference to hormone therapy, he said that there were other new agents now being used in the treatment of certain types of malignant disease. These were the substances used in the chemotherapy of cancer, and included, besides the various radioactive isotopes, the new group of cytotoxic agents, which killed or injured the growing cell by chemical or metabolic interference with certain stages of cellular reproduction. (Among these might be noted vitamin B_{12}, which appeared to cause remarkable regression in cases of neuroblastoma.) The study of the action of this group on the living cell and on isolated cell-components had recently shed new light, not only on the action of these drugs, but on the biological and biochemical events brought about by radiation itself.

It was not surprising that there were differences in the clinical effects observed with the use of these different agents, and that there were indications that certain individual drugs now being produced by Campaign workers duplicated only a part of the action of ionizing radiations. Moreover, the action of these drugs appeared to be limited to a considerable extent to definite cellular types; for instance, on either the circulating lymphocytes or on the bone marrow cells respectively. Indeed, they might even prove to be more selective than radiation therapy. "When it is remembered that only a few years ago no substance whatever was available that could be given by mouth or by injection with any hope of a favourable response in the treatment of any form of cancer, the progress to-day is abundantly evident; even though it is true that some forms of cancer are still almost as intractable as ever they were."

LORD LATHAM, in presenting the accounts of the Campaign, said that donations and collections showed an increase of £11,000 over 1952, but legacies showed a decrease of £14,000. A sum of £263,000 had been expended on grants to hospitals and research workers during 1953, and expenditure on the principal objects of the Campaign had for the first time reached over £300,000, representing an increase of 100% over the corresponding figure for 1948. The outlay on fellowships had now reached £27,420, covering 15 Campaign Fellows and an average of five Exchange Fellows to and from the United States and Canada.

The Nuffield trophy for the most successful local activity on behalf of the Campaign was presented to the Aldershot Committee.

Nova et Vetera

THOMAS BOWDLER

Though thousands of medical men have had their names become a part of medical nomenclature, the honour of eponymous commemoration yet remains a notable distinction. How much more remarkable it is, then, to have a name adopted into the common stock of the language and to be for ever associated with the greatest of the immortals, Shakespeare.

While the terms "bowdlerized" and "bowdlerism" are familiar enough, those who have paused to wonder who Bowdler was have probably, from the nature of his activities, imagined him as the male counterpart of Mrs. Grundy, an active Victorian busybody who could not let well alone. It is something of a shock to our historical sense to learn that he died twelve years before Victoria became Queen, that he was old enough to read *Tristram Shandy* when it first appeared, was 17 years old when Smollett's *Humphry Clinker* was published, and that his own "purified" Shakespeare came out at a time when the Prince of Wales, afterwards George IV, was leading popular taste in a quite different direction. That Bowdler was a doctor and, in spite of an absence of scientific attainments, a Fellow of the Royal Society is a fact unknown to or forgotten by many, and when the bicentenary of his birth is taken as an occasion for remark in a medical journal the opportunity cannot be missed of explaining, if not of excusing, the motives which led him to labour over a work which has earned for him the almost universal execration of Shakespearian scholars.

Early Days

Thomas Bowdler was born at Ashley, near Bath, on July 11, 1754. His family belonged to that class of landed gentry not usually associated with a "Pecksniffian" attitude to morals, and his parents were in fact people of culture, his mother being a direct descendant of the Sir Robert Cotton whose celebrated collection of early manuscripts is now one of the glories of the British Museum Library.

After attending a school at Claverton, near his home, he studied medicine first at St. Andrews and later at Edinburgh University, where he graduated M.D. in 1776 with a thesis on intermittent fevers. After spending four years on his "grand tour" of Europe he caught a fever while travelling to Lisbon and returned to England with his health permanently impaired. Although he was elected a Fellow of the Royal Society and a licentiate of the College of Physicians in 1781 he had no urge to practise medicine, but he occupied himself with a number of charitable causes and was one of the commissioners appointed to investigate the condition of the prisons.

His first published work was an eye-witness account of the revolution in Holland, which was at its height when he visited there in September and October, 1787. This book is still of interest to historians because of the large number of proclamations and other contemporary documents which are reprinted in it.

The standard reference works and literary histories, no doubt following the *Dictionary of National Biography* in one of its occasional errors, state that his revised version of Shakespeare was not published until 1818, but there is in the British Museum, correctly catalogued, an edition of 1807. Bowdler's name does not appear on the title-page, but a comparison with later editions leaves no doubt that the attribution is justified. Entitled "The Family Shakespeare. In four volumes," it was "printed by Richard Cruttwell, St. James's-Street, Bath, for J. Hatchard, Bookseller to Her Majesty, No. 190, Piccadilly, London." In the preface he states:

"Though the works of our immortal Bard have been presented to the public in a great variety of editions . . . I flatter myself that the present publication may still claim the attention . . . of those who value every literary production in pro-

portion to the effect which it may produce in a religious and moral point of view. . . . Few authors are so instructive as Shakespeare, but . . . his plays contain much that is vulgar, and much that is indelicate [and here he quotes from his friend, Mrs. Montagu]. On this principle I have omitted many speeches in which Shakespeare has been tempted 'to purchase laughter at the price of indecency. . . .' It is hoped that the present publication will be approved by those who wish to make the young reader acquainted with the various beauties of this writer, unmixed with anything that can raise a blush on the cheek of modesty. Twenty of the most unexceptional of Shakespeare's plays are here selected in which *not a single line is added*, but from which I have endeavoured to remove everything that could give just offence."

Popular Pastime

Modern scholars have impressed upon us the criminal nature of such purgation, but let us make sure that we are not being hypocritical about it. How many editors of school texts have been the unacknowledged debtors to Bowdler's skilful surgery? And has the B.B.C., which allows all manner of frankness in the Third Programme, never any qualms about what may be permitted in the Home Service? The question is a relevant one, for Bowdler himself, in the prefaces to later editions, emphasizes that he has produced his version for reading aloud in the home. In the days before universal compulsory education, and before the distracting range of modern entertainments came to spoil our enjoyment of the simpler pleasures, this was a popular pastime.

Bowdler tells us that he first had the idea from the memory of his father's custom of reading Shakespeare aloud to his family, and

"such was his good taste, his delicacy, and his prompt discretion, that his family listened with delight to Lear, Hamlet, and Othello, without knowing that those matchless tragedies contained words and expressions improper to be pronounced; and without having reason to suspect that any parts of the plays had been omitted by the circumspect and judicious reader."

Elsewhere he adds,

"I may venture to assure the parents and guardians of youth that they may read the FAMILY SHAKESPEARE aloud in the mixed society of young persons of both sexes, *sans peur et sans reproche*."

He reminds us that plays are always pruned for the theatre, but the play is not spoiled, and that he has attempted to do for the reader what the manager always does for the stage.

Impurities Removed

Although his work was attacked in some quarters, notably in the *British Critic*, to which he published a reply, it was widely accepted and ran into many editions. In the formidable *Edinburgh Review* the reviewer stated that

"it has in general been found easy to extirpate the offensive expressions of our great poet, without any injury to the context or any visible scar or blank in the composition. They turn out not to be so much cankers in the flowers as weeds that have sprung up by their side; not flaws in the metal, but impurities that have gathered on its surface; and that, so far from being missed on their removal, the work generally appears more natural and harmonious without them."

It is of interest to note that Bowdler's text first appeared in the same year as Lamb's *Tales from Shakespeare*, a book which was Lamb's first success and which has been beloved of generations of children. Having made quite clear what he had done and why he had done it, Bowdler earned notoriety for providing the young reader with a Shakespeare text in which it is difficult to detect the omissions; Lamb won celebrity with a brief paraphrase.

Bowdler lived at St. Boniface, Isle of Wight, from 1800 to 1810, and then at Rhyddings, near Swansea, until his death on February 24, 1825. Just before his death he finished a "purified" text of Gibbon, which was published in six volumes in 1826 by his nephew, Thomas, with the title *Gibbon's History of the Decline and Fall of the Roman Empire, for the use of Families and Young Persons, reprinted from the original text with the careful omission of all passages of an irreligious or immoral tendency.*

His only publication of any medical interest, apart from his graduation thesis, is his *Observations on emigration to France, with an account of health, economy, and the education of children* (1815). In it he warns English invalids against French spas and recommends Malta as a health resort.

F. N. L. POYNTER.

Correspondence

Dangers of E.C.T. in Cerebral Arteriosclerosis

SIR,—Dr. F. Houston (*Journal*, June 19, p. 1441) has forthrightly focused attention on the risk of relaxant-controlled electro-convulsion therapy in arteriosclerotic patients. His two illustrative cases, one fatal and the other with resultant permanent hemiplegia, expose the hazard. As suxamethonium-modified E.C.T. is in vogue our relevant experience will be briefly mentioned. Occlusive vascular disease, especially if symptomatic, is the main risk. The rare prolonged apnoea after the administration of suxamethonium may be reduced by careful attention to dose and, theoretically but not infallibly, by the use of a test-dose.[1]

The effect of drugs or other procedures, however transient, on the haemodynamics in arteriosclerosis is always an important consideration. This encouraged us[2] to determine the effect of graded doses (30–75 mg.) of suxamethonium and the associated stimulus of electroplexy on the variation in blood pressure in hypertensive and normotensive patients of varying age during routine E.C.T. It was concluded that, within this therapeutic range, suxamethonium had no clinically or statistically significant effect on blood pressure, while the shock-stimulus was mildly but consistently pressor.

We have not witnessed any vascular catastrophes attributable to this treatment. Since hemiplegia may develop during hexamethonium treatment in arteriosclerotic, hypertensive patients, we have not ventured to use this latter drug as a preparatory to E.C.T. Again, hydralazine ("apresoline"), with its attendant mental depression, is not particularly suited, but reserpine, although a weaker hypotensive agent, is comparatively safe and mildly euphoriant, both useful considerations. We rarely use hypotensive agents in arteriosclerotic, hypertensive patients undergoing thiopentone-suxamethonium-oxygen-modified E.C.T. Reasonable assessment of the risk with this technique for these patients includes: history of cerebral, coronary, or peripheral vascular symptoms or signs; detailed physical examination of the cardiovascular and nervous systems: with teleradiograms usually and electrocardiograms occasionally. Reasonable justification for this treatment is obtained when consultation between psychiatrist, physician, and anaesthetist permits a full appreciation of the hazard, maximal safeguard against it, discrimination in the selection of patients, and a critical examination of the safety of the technique adopted.—We are, etc.,

ROWLAND J. CALVERT.
DEANE K. MORGAN.

London, E.11.

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Fractures Complicating E.C.T.

SIR,—I was interested in your annotation on "Fractures Complicating E.C.T." (*Journal*, June 19, p. 1428). I, however, consider that your article might have dangerous repercussions on the use of this valuable means of treatment in psychiatric practice. The references quoted giving such a high incidence of fracture which varied from 23% to 35.4% are hardly an inducement to continue this treatment. The reported incidence of such injuries among patients receiving electro-convulsive therapy varies considerably. In a recent publication[1] a study of 2,200 patients receiving electro-convulsive therapy showed that there was an overall in-

cidence of injury of 2.4%, and this included fractured spine, femur, shoulder, and dislocated jaw. The incidence of fractured spine was only about 1%.

With regard to their prevention, I have not seen a case of fracture or dislocation when electro-convulsive therapy was carried out with the use of the muscle-relaxant drugs.—I am, etc.,

Lancaster. J. P. KELLY.

REFERENCE

1 *J. Bone Jt Surg.*, 1954, 36B, 70.

Intravenous Acetylcholine in Neuroses

SIR,—The article by Drs. R. M. Phillips and J. T. Hutchinson on acetylcholine in neuroses (*Journal*, June 26, p. 1468) is of great value in more than one respect. It contributes to the problem of physical remedies in neurotic conditions, a sphere in which, happily, increasing progress has been made. Another service is rendered through pointing to the difference between tense obsessive states and obsessive-compulsive neuroses. For years I have tried to draw attention to this fact at meetings and in conversations. Young psychiatrists in particular have responded with wide-eyed surprise, incredulity, or indifference. The psychoanalytical literature they read, as well as writings by "organotherapists" and psychiatric sceptics, pay no attention to this substantial difference. Much futile psychoanalysing and abreacting would be avoided, and appropriate supportive psychotherapies devised, if the distinctness of the tense obsessive disease were appreciated. Admittedly, even within this group there are differences in pathological dynamism and presenting features. Some patients, after having failed with acetylcholine, benefited from ordinary hypno-suggestion, even though, as expected, only superficial somnolence could be achieved.

This is not the place for outlining and explaining the distinctive aspects of various obsessive pictures. However, the planning of treatments would be much aided by keeping in mind a few pertinent observations. I should be glad if these comments reached the attention of young psychiatrists working in the comparative seclusion of provincial mental hospitals, and without the opportunities of personal contact with a variety of experienced psychotherapists. Painstaking research into the problem would be rewarding, and result in the gratitude of many patients now being doomed to disillusionment because of futile attempts at treating them.—I am, etc.,

London, N.W.4. SAMUEL LOWY.

Metabolic Effect of Salicylate

SIR,—The recent publication by Dr. J. B. Cochran (*Journal*, March 27, p. 733) on the metabolism-stimulating effect of salicylate, together with a subsequent report by Dr. B. W. Meade (*Journal*, April 17, p. 936) on the inability of γ-resorcylic and meta- and para-hydroxybenzoic acids to increase oxygen consumption in the albino (Wistar) rat, prompted us to report the results of some of our own experiments.

Because of the suggestion that the metabolism-stimulating effect of salicylate might be of fundamental importance in the therapeutic action of the drug,[1] we investigated the effects on oxygen consumption of other drugs that have been employed in, or suggested for, the treatment of rheumatoid conditions. It was realized that the extension of Cochran's suggestion to cover all anti-rheumatic drugs, whether or not they bear a chemical resemblance to salicylic acid, implied that all therapeutically effective anti-rheumatic compounds have at least some pharmacological action in common. The notion was considered sufficiently interesting to warrant investigation.

The compounds were administered to albino rats of either sex (W.A.G. strain, body weights 130 to 180 g.), or to groups of fawn mice (G.F.F. strain, body weights 15 to 22 g.). Determination of oxygen consumption rates by a modified Maclagan and Sheahan technique[2] began approximately 30 minutes later. It was observed that γ-resorcylic acid, gentisic acid, methoxy aspirin,[3] salicylamide, polycondensed hexahydroxy "trigentisic acid,"[4] 2.2′:5.5′-tetrahydroxy-3.3′-dinitro-diphenyl,[5] butazolidine, and meta- and para-hydroxybenzoic acids did not raise oxygen consumption, whereas salicylic acid and acetylsalicylic acid did. This inability of the two isomers of salicylic acid is in agreement with both Meade's and Cochran's findings. Neither isomer is of any therapeutic value in rheumatic fever.

In addition, it is noteworthy that neither cortisone acetate nor cinchophen increased oxygen consumption. Although cinchophen fell into disrepute on account of its hepatotoxic action, it was nevertheless most effective in the therapy of rheumatic fever. Likewise the value of cortisone in this field needs no emphasis. It follows, therefore, that if the stimulating effect on oxygen consumption is an essential pharmacodynamic action of salicylates, then cortisone and cinchophen must differ from salicylates in their modes of action.

Our attempts to correlate the above recorded effects on oxygen consumption with the clinical efficacy of the drugs have not been successful. We have found that drugs of well-established action, such as acetylsalicylic acid and salicylates, have an enhancing effect on oxygen uptake: in contrast this property was not shown by other recognized anti-rheumatic drugs—cortisone, for example.—We are, etc.,

DAPHNE E. HALL.
E. G. TOMICH.
E. A. WOOLLETT.

Greenford, Middx.

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4 Hahn, L. (1952). *Nature, Lond.*, 170, 282.
5 Forrest, J., *et al.* (1952). *J. Pharm. Pharmacol.*, 4, 231.

Cortisone and Aspirin in Rheumatoid Arthritis

SIR,—It is agreed that statistical analysis is essential to scientific progress, and as a profession we owe a debt to Professor Bradford Hill for his work in its application to medical problems; but the claim that clinical observation can be co-ordinated effectively in any statistical survey is illusory. For example, the interaction between emotional states and endocrine activity is universally recognized, but, in the present state of our knowledge, not subject to assessment. In the Medical Research Council's investigation (*Journal*, May 29, p. 1223) an effort is made to eliminate this psychological element by presenting the aspirin as an unrecognizable brown tablet; but inevitably these 31 patients were led to think that as subjects of a special investigation they were being given some obscure or modern drug, and thereby gained the psychological impetus of hope and faith; had a correlative number been told frankly they were being treated by aspirin, I venture to think that the results would have been vastly different.

We may as well recognize that the imponderables are in fact imponderable, and that *ex cathedra* pronouncements have value as statistical findings, and no more; otherwise we shall shortly be attempting to express the desire of the moth for the star in terms of πr^2.—I am, etc.,

Sunderland. W. GRANT WAUGH.

Periarthritis at the Shoulder

SIR,—We should all welcome the paper by Mr. N. J. Blockey, Mr. J. K. Wright, and Mr. J. H. Kellgren (*Journal*, June 26, p. 1455) as indicating one more limitation of systemic treatment by cortisone for a localized lesion. I agree with them that oral cortisone is of very doubtful benefit in capsulitis at the shoulder. But it is worse than that; it is unsuitable treatment. Though discussion continues on whether or not treatment with this hormone is called for when many joints are affected, a direct approach clearly becomes possible when only one joint is involved. Local anti-inflammatory action is most easily secured by injection of small amounts of hydrocortisone into the joint itself. There is then a strong local concentration without fear of systemic effects, however long treatment has to continue.

The capsular lesions at the shoulder that satisfy the authors' criteria fall into four categories—traumatic arthritis, freezing arthritis, osteoarthritis, and monarticular infective arthritis. Though superficially similar, their clinical course and susceptibility to treatment differ widely, as does their response to intra-articular hydrocortisone.[1]

In freezing arthritis and osteoarthritis the hormone is ineffective and in traumatic arthritis only sometimes beneficial. By contrast, infective arthritis treated by local hydrocortisone provides one of the happiest results in the whole sphere of orthopaedic medicine. The patient, worn out by months of pain and broken sleep, loses all discomfort within 36 hours. A first injection of 25 mg. usually lasts him a week. Though the range of movement does not increase to begin with, sleep and freedom from pain transform the patient overnight. I hope, therefore, that the poor results of oral cortisone when these separate disorders are treated together will not militate against further research on the lines suggested above.—I am, etc.,

London, W.1. JAMES CYRIAX.

REFERENCE

[1] Cyriax, J., and Troisier, O. (1953). *British Medical Journal*, 2, 966.

Homosexuality

SIR,—Of course Dr. Clifford Allen (*Journal*, June 19, p. 1442) and Dr. G. G. Sherriff (*Journal*, June 26, p. 1496) are right. The Napoleonic Code is the most sensible way of dealing with the social aspect. Public opinion in the countries where it is in operation, tolerant if slightly contemptuous, renders homosexuals an inconspicuous and inoffensive minority. I see no reason why it should not do so in the United Kingdom. The fixing of an "age of consent," say 20 or 21, would greatly lessen the risk, feared by Dr. R. Cove-Smith (*Journal*, June 26, p. 1496), of young men suffering corruption and a short-circuiting of their emotional development.

Is there, by the way, any evidence that a normal person can be *permanently* deviated into "unnatural" channels? I have long thought that too much fuss is being made over the whole problem. Investigation of the condition and treatment where it is likely to help are urgently needed. One should, however, retain some sense of proportion. The increased police activity does not necessarily mean that homosexuality has increased. All it may mean is that the police are taking more notice of it.—I am, etc.,

London, N.W.8. F. G. MACDONALD.

SIR,—It may be the duty of the Churches and other public groups to do all they can to restrict and suppress what they consider to be evil conduct, and the views of those who, like Dr. C. G. Learoyd (*Journal*, June 5, p. 1326), hold that homosexual practices are "immoral or evil or deadly sin, and filthy and just as foul by whatever name they are called," must be respected, but it is not the duty of the State to interfere in questions relating to the morality of personal behaviour, and it is intolerable that persons can still be pilloried and prosecuted solely on moral grounds.

In most so-called civilized countries sex has become a source of evil partly because it has been denied the opportunity of natural development. Instead of blooming like a rose, sex often grows like a fungus in secret places. Children are still being brought up to be ashamed of their genital organs. Until recently masturbation was considered to be a deadly sin, one form of treatment for which was circumcision without anaesthesia. In his book, *An Apple a Day*, Dr. P. Gosse[1] describes in terms of disgust the public exposure and expulsion, which he witnessed at school, of a boy found guilty of the "crime" of masturbation. Dr. Learoyd obviously includes "mutual masturbation" in the practices which he describes as "immoral or evil or deadly sin, etc." I wonder what he thinks of the answer given in the "Any Question?" column (p. 1335) of the issue of the *Journal* in which his letter appeared to the question entitled "Masturbation in a Married Woman"?

It is wrong that court proceedings in sexual cases should receive such incontinent publicity; this adds considerably to the punishment of convicted persons, as well as to the suffering of innocent relatives. Until the general public can regard the problem of sex more objectively and with less hypocrisy, persons convicted of sexual "crime" are faced with the prospect of becoming social outcasts. They are also liable to a particularly cruel and cowardly form of abuse from persons who profess such views as does Dr. Learoyd, and it is not to be wondered at that some of them find release from their sufferings in suicide. The morality of certain forms of sexual behaviour is a matter for individual conscience, but who can question the unfairness of the attack recently made in the House of Lords on a certain public figure?

The type of publicity already referred to constantly exposes young people to unhealthy sex propaganda which must tend to impress on their minds the association of sex with sin, instead of with marriage, procreation, and happiness. There is no reason why children should not grow up in ignorance of unnatural forms of sexual expression. While denying the right of consenting individuals to behave in certain ways in private, the State then tolerates this immoral propaganda in the name of "the freedom of the press."

No doubt there have been signs in recent years of a more tolerant attitude towards the problem of sexual conduct, and, thanks largely to the work of medical experts, a revision of ideas relating to the dividing line between normal and abnormal sexual behaviour has been made on the basis of knowledge and understanding rather than of prejudice and emotion. The problem before the Home Secretary's committee will concern not only homosexuality but the fundamental question of sex and freedom in an organized society, and it is to be hoped that the views of the medical profession on this vital issue will be made known.—I am, etc.,

Barnet, Herts. W. B. LAING.

REFERENCE

[1] *An Apple a Day*, 1948. Cassell.

Smoking and Cancer

SIR,—With reference to the article "The Mortality of Doctors in Relation to their Smoking Habits" (*Journal*, June 26, p. 1451), I feel that there are many other conclusions which could be drawn from the figures given, apart from the conclusions reached in the article. According to the figures in the article, the deaths from lung cancer amongst all smokers were 36 when the expected deaths should only have been 32–26. This is stated to be a statistically significant increase and justifies the conclusion that smoking is a definite factor in the production of lung cancer, but, if that is so, then surely a death rate of 15 amongst non-smokers from other cancers, when the expected death rate should only have been 10.1 is also statistically significant and would justify a conclusion that smoking in some way protects the individual from other cancers. In my opinion, neither conclusion is the correct one. If one collects the deaths from all cancers together, including lung cancers, I think one gets the answer and one finds that the expected deaths and the actual deaths from all cancers, both amongst smokers and non-smokers, becomes the same.

Deaths from All Cancers

	Non-Smokers	All Smokers	Total
Observed deaths	15	113	128
Expected deaths	13·9	114·1	128

In short, a smoker is no more liable to die of cancer than a non-smoker. A smoker is more liable to get his cancer in the lungs, but he gets the compensation that he is less liable than the non-smoker to get it elsewhere. This finding is in accordance with other investigations on cancer. For example, in areas where vesical bilharziasis is prevalent,

carcinoma of the bladder is also prevalent, but I have always understood that in these areas the increased death rate from carcinoma of the bladder is compensated for by a decrease in the death rate from cancers in other sites.

I realize that the writers of the article are well aware of all this, but they have not stressed it, and their article has been widely quoted in the lay press, and the lay press has given the impression to the public that smokers are much more liable to die of cancer than non-smokers, thus producing a certain amount of anxiety amongst smokers, whereas in fact, from the evidence so far available, they are no more liable to die of cancer than non-smokers, but only more liable to get their cancer in the lungs.—I am, etc.,

Bradford. ROY F. FAIRWEATHER.

SIR,—The article, "The Mortality of Doctors in Relation to their Smoking Habits" (*Journal*, June 26, p. 1451), lends support to the belief that excessive tobacco smoking is associated with a rise in the incidence of lung cancer. It is sometimes worth while seeing if an experiment, designed to answer a specific question, contains the answer to another question not asked when the experiment was designed. I would like to ask the question, "Is non-smoking associated with any evil thing?" It would seem from Table IV and the chart that the answer is yes. Non-smoking is associated with a greater mortality from all cancers than moderate smoking. Do Dr. Doll and Professor Bradford Hill regard these figures as statistically significant? If they do it is an important observation. It would indeed be a tragedy if, as a result of the fine work that has gone into this problem, many moderate smokers transfer themselves to the category of non-smokers associated with a higher death rate from cancer.

The experiment seems to confirm the dull hypothesis—moderation is a good thing.—I am, etc.,

Wadhurst, Sussex. GEOFFREY E. LOXTON.

Cytodiagnosis of Bronchial Carcinoma

SIR,—I should like to support Dr. F. Hampson's views (*Journal*, June 26, p. 1495) on the value of cytodiagnosis in bronchial carcinoma. As he says, "Many tumours are beyond the reach of the bronchoscope." It is probably true to say the majority, especially in their early stages. It is especially in these cases that sputum examination is of value and does on occasion produce surprises.

But it is not only in cases where the tumour is beyond bronchoscopic vision that the cytodiagnosis may be of value. I have recently had a case in which bronchoscopy showed a tumour-like protrusion into the bronchus, a biopsy section of which showed no evidence of malignancy but only chronic inflammatory reaction. Sputum examination, however, showed the presence of carcinoma cells. The patient was operated upon and had his lung and carcinoma removed. Without the sputum examination his condition would have been labelled inflammatory.

I do not understand why Dr. R. Whitehead (*Journal*, May 29, p. 1254) should think that it is a waste of money to train pathologists and technicians to look for malignant cells, but worth while to spend money on training bronchoscopists and their assistants to do bronchial biopsy, which is also a skilled and expensive procedure.—I am, etc.,

Mundesley, Norfolk. EVAN WYNNE-EDWARDS.

Amphetamine Addiction

SIR,—In connexion with Dr. R. B. Carr's case report "Acute Psychotic Reaction after Inhaling Methylamphetamine" (*Journal*, June 26, p. 1476) I think that the following case is of interest.

A man, aged 42 years, became addicted to amphetamine in 1949. There is a family history of nervous instability, and he was pampered and spoilt as a child. He was rejected from military service in 1939 on account of his "nerves." In 1946 he inherited a considerable sum of money and became a heavy drinker. In 1949 he began to break open "benzedrine" inhalers, and would either suck the enclosed stick or soak it in a cup of water and drink the resulting suspension. He was soon using up to three inhalers each day, and in one month his wife was able to collect 72 opened and empty inhalers. His behaviour deteriorated progressively, he became aggressive and paranoid, and in 1952 he was admitted to a mental hospital under an urgency order, the diagnosis made there being "benzedrine addiction with superadded paranoid psychosis." He responded well to sedation and withdrawal of the amphetamine, and became well adjusted to home life. However, he was soon taking the drug in the same way, and, when I first met him in February, 1954, was deteriorating again in behaviour. He was uncooperative and refused treatment. In May, 1954, he again developed an acute psychosis with delusions of persecution and violence, and had to be admitted again to a mental hospital under an urgency order. He is now improving rapidly, though no doubt he will relapse once more after discharge.

The amphetamine group of drugs is in Schedules 1 and 7 of the Poisons Rules, but is exempt from restriction when used for inhalation, though the "benzedrine" inhaler contains 325 mg. of amphetamine, and the "methedrine" inhaler used by Dr. Carr's patient 250 mg. of methylamphetamine. Dr. Carr states that "there have, of course, been many cases of addiction and even of psychosis associated with the ingestion of amphetamines, and in this connexion inhalers are often used as a ready source of the solid drug." In our practice there is another, milder, amphetamine addict—she obtains "methedrine" tablets by signing the chemist's poisons book, and is unable to do without their stimulating effect.

It would be interesting to know if other doctors have similar cases in their practices, for I think that this form of addiction may be more common than is supposed. I feel that the uncontrolled sale of this drug of addiction in such large doses for inhalation is both dangerous and unnecessary. There are other vasoconstrictors which serve equally well and are relatively harmless. If one recognizes amphetamine and its derivatives as drugs of addiction, which they surely are, the logical solution is to place them into Schedule 4 of the Poisons Rules (which, besides controlling their sale as tablets, would, I believe, automatically prohibit their uncontrolled sale in inhalers), and I think that this is the solution to the problem.

I am indebted to Dr. A. S. Ogden for permission to report this case.—I am, etc.,

Bournemouth. R. G. NICHOLSON.

Carcinoma and Neuropathy

SIR,—Since my previous letter on this subject was published in your columns (*Journal*, May 15, p. 1155) I have had the opportunity to study the paper by Dr. R. A. Henson, Professor Dorothy Russell, and Dr. Marcia Wilkinson,[1] to which Dr. Henson refers in his letter (*Journal*, June 5, p. 1323). In his earlier report[2] Dr. Henson remarked that one patient "differs from the others in that he has no clinical sign of any nervous lesion and the picture is that of a subacute myopathy or polymyositis." He later goes on to say, in considering differential diagnosis: "Dermatomyositis is the condition which most closely resembles this syndrome."

Although our difference may be largely one of terminology, I do not believe that Dr. Henson and his co-workers, in their exhaustive and interesting report,[1] have produced sufficient evidence to support his comment that "in no case did we find pathological evidence of dermatomyositis or polymyositis." In view of the somewhat indefinite nature of the muscular changes which they observed, they refer to the condition in those patients whose complaint was predominantly muscular, and not neuropathic, as a "carcinomatous myopathy." However, the principal muscular lesion which they describe—namely, necrosis and active phagocytosis of scattered muscle fibres—is sometimes practically all that may be seen in subacute cases of polymyositis,

in which cellular infiltration, and vascular, connective tissue, and skin changes may be lacking. It is unfortunate that no mention is made of the presence or absence of regenerative phenomena, which are seen to a greater or lesser extent in practically all such cases.[2] I would, of course, agree with Dr. Henson, Professor Russell, and Dr. Wilkinson that similar pathological changes in muscle may occasionally be seen in other diseases, since muscle tissue can have only a limited repertoire of response to a variety of noxae. Polymyositis, after all, is a term used to describe a particular clinical syndrome which is associated with certain pathological changes in muscle. Although it is evident that in many cases the disease process shows an affinity with the other collagen-vascular diseases, this may not be true at all, and it is possible that many different agents may be of aetiological importance. However, I believe that the time is approaching when we must discard the concept of dermatomyositis or polymyositis as an acute disease accompanied by striking inflammatory changes in both skin and muscle and realize that the process may be much less dramatic both clinically and pathologically. Skin changes, pain, and tenderness may be entirely absent, and the condition may present with variable and remittent muscular weakness of proximal distribution; there now seems little doubt that the cases described by Shy and McEachern[4] as "menopausal muscular dystrophy" were in reality examples of polymyositis.[3] The same may well prove to be true of at least some of those cases which Dr. Henson and his colleagues have described as "carcinomatous myopathy."—I am, etc.,

Boston, Mass. JOHN N. WALTON.

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[4] *J. Neurol. Neurosurg. Psychiat.*, 1951, 14, 101.

"Sulphatriad" Anuria

SIR,—The use of three sulphonamides in combination is claimed by some manufacturers to reduce the incidence of complications of chemotherapy. Though this has not been proved, it is a good idea. Unfortunately one of the sulphonamides often chosen is sulphamerazine. Sulphamerazine is poisonous and produces crystals in the renal tract leading to haematuria and blockage, as reported by Mr. M. D. Sheppard (*Journal*, January 10, 1948, p. 73); by Mr. Ashton Miller and Mr. J. P. Mitchell (*Journal*, September 27, 1952, p. 705); and others from time to time.

"Sulphatriad" contains 26% of sulphamerazine. During the past two years I have seen two cases of severe haematuria and anuria following the use of normal doses of sulphatriad, and I have reason to believe that other cases have occurred.

Is it too much to ask that the manufacturers will co-operate in removing this toxic drug from their mixtures in the same way that calomel has been removed from teething powders?—I am, etc.,

Bath. HUGH R. E. WALLIS.

Proposed Coat of Arms for B.M.A.

SIR,—I was very interested in the proposed coat of arms for the British Medical Association (*Journal*, June 26, p. 1491). May I make one or two comments?

In the blazon should the Lion not be armed and not horned? The motto is, I think, somewhat unfortunate because the word "salus" is often taken to refer to the safety of a people; and the motto has unfortunate associations, for it is often used to justify unconstitutional acts or immoral acts in an emergency, and it suggests that the safety of the nation is more important than the moral law. The coat of arms is very English. I think it is right and proper that the Hastings Maunche should be introduced. Harvey is also a suitable supporter, but I would suggest that the yellow English Lion should be replaced by, say, the Rose, the Thistle, and the Leek (proper on argent). These are royal badges and would suitably represent our gracious patron, the Queen. Is it intended in any complete reproduction to have a helmet? Meantime the crest rests on a wreath without a helmet. I would suggest that the Lord Lyon King of Arms of Scotland also be consulted in the matter.—I am, etc.,

Aberdeen. JOHN CRAIG.

SIR,—The proposed coat of arms for the British Medical Association, as illustrated in the *Journal* of June 26 (p. 1491), may have significance in its composition and may be faultless in heraldic detail, but as a work of art it is atrocious.

Taking part by part, the shield itself is the only component well conceived, and the fact that "per pale" it is presented in the colours of one of our leading teaching hospitals adds for many a certain nostalgic dignity. Apart from the commendable associations with the House of Hastings, the Maunche serves as an everlasting reminder that our pocket can never be divorced from our noble work. The Lion is a happy choice for the "in chief" position, and red for blood and gold for laudable pus are appropriate indeed. The crest, however, is terrible and only equalled by the clumsiness of the supporters. The former is grotesquely top-heavy and out of all proportion to the shield below; while the latter are overpowering and dull. The motto, though appropriate enough, is hardly original, but I would not condemn it on that score.

There is much to be said for having a coat of arms, as Dr. S. F. Logan Dahne has stated in his explanatory note, but please let us have something beautiful and delicate; something which bears the hallmark of artistic inspiration as well as scholastic industry. The monstrous composition, as illustrated, though full of the latter, is sadly wanting in the former, and I earnestly hope that other suggestions will be invited and considered before a final choice is reached.—I am, etc.,

Hambleden, Oxon. JOHN ELLIOTT.

SIR,—Dr. S. F. Logan Dahne's article on the proposed coat of arms for the British Medical Association (*Journal*, June 26, p. 1491) was full of dogmatic fiction.

The excuse for using the maunch is not very convincing. One cannot but be distrustful of the statement that Sir Charles was a "cadet branch" of the great mediaeval House of Hastings when no evidence is put forward other than the fact that he had "a lovely silver tray" with similar arms engraved upon it. Heraldry, both accurate and inaccurate, was a popular Victorian pastime. If indeed he was a cadet of the noble Hastings, one is surprised that he made no claim to any of the ancient baronies of that family that would have been his rightful inheritance and which failed for lack of male heirs. Even in the sometimes optimistic Burke's *Landed Gentry* (1921 edition) not only does Sir Charles's family make no claim to any antiquity of descent—the pedigree starts with his father—but no armorial bearings of any sort are claimed.

On a chief gules is a golden lion passant, and very handsome it looks. But Dr. Dahne makes the extraordinary assertion that "no one can use the Royal Lion, which is Her Majesty's personal property." This begs the question as to whether the leopards of England should ever be called Lions, but, more importantly, the assertion is quite untrue. A great many families bear, on gules, either the golden lion or leopard passant. Several such grants of arms can be found among the grants of Garter Sir Edward Walker (British Museum MS. 37675). The torse or twist, Dr. Dahne states, "was always in [the] main colours." There is no truth in this assertion; a vast number of examples could be cited where the torse colours appear to bear no relationship with the colours of the arms. In a few cases, indeed, more than two colours are employed.

In the last paragraph Dr. Dahne tells us how the full achievement should be heraldically described: "*Shield.*—Per pale, or and azure, a Maunche counterchanged, in chief gules a Lion Passant of the first, horned and langued of the second." Apart from the bizarre sprinkling of capital letters this description is also open to criticism. It seems

from the picture that "on a chief" is intended instead of "in chief." And where are those horns that Dr. Dahne claims to have seen ?—I am, etc.,

Ipswich. EDWARD ELMHIRST.

Cardiac Infarction and Peptic Ulcer

SIR,—Mr. P. A. Lane Roberts's article on eight cases of peptic ulceration complicating surgery and trauma (*Journal*, June 5, p. 1295) prompts me to report briefly two cases from a series of 55 acute myocardial infarctions, admitted during the past year to one of the medical units at the West Middlesex Hospital. They are of interest in view of the apparent association of haematemesis and/or melaena with acute myocardial infarction, in one case with fatal outcome.

Case 1.—A woman of 84, admitted in June, 1953, under the care of Dr. M. M. Deane, gave a history of recent myocardial infarction as well as of dyspepsia of 30 years' standing. Presence of a gastric ulcer had been proved some years previously. She was not in congestive failure and E.C.G. confirmed recent anterolateral infarction. On the eighteenth day of treatment with ethyl biscoumacetate ("tromexan") she had a severe haematemesis (Hb 55%). She was transfused immediately and thereafter made an uneventful recovery.

Case 2.—A man of 62 was admitted in April, 1954, under the care of Dr. P. M. McAllen with symptoms of recent coronary thrombosis. He gave no history of dyspepsia. There was no evidence of congestive failure and E.C.G. confirmed recent anterior myocardial infarction. On the twelfth day of treatment with phenylindanedione ("dindevan") he passed a melaena stool and later had repeated small haemataemeses (Hb 67%). Despite intravenous vitamin K_{12}, etc., he continued to deteriorate and died next day. Necropsy revealed a chronic duodenal ulcer with recent acute haemorrhage and recent apical cardiac infarction.

This series also includes two cases with known peptic ulcers, similarly treated with anticoagulants for their cardiac episodes, yet showing no overt clinical evidence of bleeding from their gastro-intestinal lesions during the first three weeks of treatment. May I suggest that the two cases with bleeding episodes represent stress reactions following severe medical "shock" similar to those described by Mr. Lane Roberts after surgery or trauma? It is important to be fully aware of this type of complication occurring within the first three weeks of treatment, because of the associated serious prognosis—that is, four cases with two haemorrhages and one death. Sudden haemorrhage with its concomitant fall in B.P., in a patient whose myocardium is already damaged by infarction, must inevitably worsen the chances of recovery.

It was further observed in this series that a proportion of patients complained of epigastric pain or indigestion, relieved by alkalis, at some time during the first three weeks of their treatment without clinical evidence of congestive failure or hepatic enlargement. This may well indicate the occurrence of acute peptic ulceration or acute exacerbation of a pre-existing lesion. It would be difficult to prove this supposition, as a barium meal could only be performed with safety at a much later stage, by which time the lesion may well have healed and the result be negative. Gastroscopy would reveal the presence of a gastric lesion, but is not a procedure advisable so soon after myocardial infarction. Examination of gastric contents for the presence of blood or faecal occult blood estimations are possible avenues of exploration without involving undue disturbance of the patient.

A history of chronic indigestion or proved peptic ulceration should always be inquired for and duly noted in cases of myocardial infarction. It does not appear to be a contraindication to anticoagulant therapy, as bleeding does not invariably occur in these cases, but should be a warning to be on the look-out for sudden massive gastro-intestinal haemorrhage in a patient whose blood-coagulating mechanism is already severely impaired.

A further report dealing with this, and other complications of anticoagulant therapy, etc., will be published in the near future.—I am, etc.,

Isleworth, Middx. P. S. ELIAS.

Obituary

H. A. DUNLOP, M.Sc., M.D., F.R.C.P.

Dr. H. A. Dunlop, consultant physician to Charing Cross Hospital, died at his home in London after a long illness on July 2. He was 50 years of age.

Hugh Alexander Dunlop was born on August 31, 1903, the younger son of David and Marion Dunlop, of Ayrshire. From Midhurst Grammar School he went on to King's College, London, and the Westminster Hospital, where he was Guthrie Scholar. He also gained the Chadwick prize, the Frederick Bird gold medal and prize, and the Abraham's prize. After qualification in 1924 he held a number of appointments at the Westminster hospital, including those of house-physician, house-surgeon, assistant medical registrar, and medical registrar. In 1927 he graduated M.B., B.S., and proceeded to the M.D. in 1932 and to the M.Sc. in 1934. He became a Member of the Royal College of Physicians in 1930 and was elected F.R.C.P. in 1938.

Dunlop always had a keen interest in physiology, and after graduation he held a Berridge Research Studentship in applied physiology, a University Studentship in physiology, and he was also a demonstrator of physiology at King's College. On the resignation of Dr. W. J. Adie in 1935 he was appointed physician to out-patients at the Charing Cross Hospital. Among previous appointments which he had held were those of physician to the Metropolitan Hospital, assistant physician to the Royal Waterloo Hospital, and neurologist to the Marylebone Children's Clinic. He was elected a Fellow of King's College in 1948. Dunlop's special interests as a clinician lay in endocrinology, neurology, and psychiatry, and he had published a number of papers in this and other journals. At the time of his death he was medical tutor at Charing Cross Hospital, lecturer in applied physiology at King's College, and examiner in pharmacology to the universities of London and Cambridge. He is survived by his widow and three sons of the marriage.

Dr. PHILIP ELLMAN writes: It was not until September, 1939, that I came to know Hugh Dunlop closely, when he and I were directed to the Leatherhead Emergency Hospital, part of the King's College Hospital sector. Billeted with him at the local golf club, I came to know him in all his moods and aspects, alternately stimulating and provocative, counselling and persuasive. His brilliance was indeed many-sided. He had a great clinical reputation, and a generation of King's College and Charing Cross Hospital students has borne testimony to his ability as a lecturer. In establishing with him and the late Dr. Douglas Firth a department of medicine at the Leatherhead Emergency Hospital I became aware of his practical ability and of his far-sightedness in matters of organization.

His interests extended to many spheres, and his life was a complete and integrated whole. His knowledge of the classics, of the Bible, and of the literature and languages of many lands was evident throughout the course of daily routine, which he enlivened constantly with his scintillating wit. And yet, although none of us was his peer, he never made us feel small nor did he sharpen his wit at our expense. Hugh Dunlop had no conceit in him and his unselfishness enabled him to be a friend to even the most simple of us. To have known him was to have had one's own life enriched. Outstanding among his many qualities were his loyalty and his fundamental kindness. He was able to project himself into other people's situations, and it was partly for this reason that psychiatry appealed so

greatly to him. His other great interests in medicine were endocrinology and neurology, but he was, first and foremost, a general physician—he would have been irked by any more restricted sphere, and departmentalism was the very negation of his broad vision. There were so many facets to his personality that he will be mourned by friends in many and various walks of life.

Dr. P. P. DASER died on June 3, after a life devoted to the medical service of Tyrol. Peter Paul Daser was born at Innsbruck in 1877. He graduated at the University of Innsbruck in 1902, and after a year's voluntary military service came to London as house-surgeon at the German Hospital. In 1906 he acquired the conjoint diploma of the Royal Colleges and practised in the City. His wife, formerly Miss Constance Hoare, was English. At the outbreak of the war in 1914 he had to leave England—a country to which he had become greatly attached and which he loved for the rest of his life. We are indebted to Dr. F. PARKES WEBER and Dr. MITTERSTILLER, of Innsbruck, for the following appreciation: During the first world war Dr. Daser served mostly on the South Tyrol front, and for his care and efforts for the wounded soldiers he was awarded several imperial orders. After the war, in 1923, he entered the public health service of Tyrol, having passed the appropriate examination with distinction, and later became inspector and then director of the service. His work for invalids and his struggle against the epidemic of paratyphus in Innsbruck in 1932 were recognized by the Austrian Ministry of Health, and the title of "Hofrat" was conferred on him in 1934. Dr. Daser then occupied for many years a leading position in his country's health service. He was a man of kindness, justice, and correctness. With great dignity he bore the disregard shown him after 1938, when he had to yield to brutal force. As a good Austrian, whose father had fought in the ranks of the Emperor Maximilian in Mexico, he would have nothing to do with the new regime. Later on Hofrat Daser was reinstated, and at the end of 1946 he retired. The University of Innsbruck had planned to celebrate the fiftieth anniversary of his graduation just before his death. During his practice in London I did a little literary work with him, and he was always helpful and ready with his translating.—F. P. W.

The death of Dr. JOSEPH WASSERSTEIN on June 17 has robbed Stoke Newington, Tottenham, and the surrounding area of a much-respected figure. He came to medicine at a relatively late age, qualifying from the London Hospital in 1927, but he brought to it a mind all the more cultured and keenly trained. He died of a heart attack which followed his going out in the middle of the night to attend another doctor's patient, and it was typical of his modesty that this fact was elicited only through the taking of a detailed history as he lay very ill. He remained a student to the end, attending assiduously lectures, clinical rounds, and refresher courses—this when he was in his sixties. The City Division has lost a good member, his patients a cultured and kind doctor, and many of us a lively friend. Our sympathy is extended to his widow and his two children.—C. S.

Medical Notes in Parliament

TREATMENT AND WELFARE OF SPASTICS

The report on the special welfare needs of spastics, published last December by a special subcommittee of the Advisory Council on the Welfare of Handicapped Persons, was the basis of a discussion in the House of Commons on June 28.

Mr. HORACE KING (Southampton, Test, Lab.), urging the report should be carried out, said that the chairman, Dr. Evans, and others had made it a first-class document that was nearly as good as the excellent work the individual members of the committee had themselves done for spastic children. The important thing was to co-ordinate all the departments concerned with the well-being of spastics and to see that the job of looking after them was treated as a whole, locally and nationally. Spasticity was so definitely a matter of expert knowledge and medical science that the medical officer of health locally and the Minister of Health nationally should be made the factors linking all the Government offices dealing with spastics.

More special schools were needed at once; the national provision was pitifully inadequate. There were between 6,000 and 12,000 spastics of school age, and there were places at special schools for 169—although other special schools for handicapped children provided for some spastics. More spastic centres to which children could be taken daily for treatment, diagnosis, and education were needed, and an adequate number of home teachers for those who could not be moved. Welfare work must be widened to help the spastic to earn his own living if it was possible. In every large town, near the physiotherapy unit, there should be a spastic centre. Work by the expert in the unit could be followed by personal contact between parents and consultant.

Mr. IAIN MACLEOD, Minister of Health, said that although the number of spastic children might be small they represented a challenge to humanity and ingenuity. The report was of great significance and value, and he had already taken the first step to follow up the admirable initiative which the committee had given. In January he asked medical officers to include in their reports for 1953 certain information which would be of value. He had asked them to tell him about the incidence of these cases in their areas, about which the evidence was a little conflicting; to review the facilities for these handicapped persons; and to state what was being done about co-ordinating all the various bodies who had a share in the work. The reports this year would not be complete, but they would give a preliminary picture.

He was satisfied that in many areas research was being done, and was reaching down into the hospitals; and the new Clinical Research Board would help a great deal. Co-ordination had been his theme song in all speeches about the Health Service. Co-ordination of hospital and welfare provision, the education service and the local authorities, was obvious enough, but it was not so obvious—and he was glad the report pointed it out—that a fully comprehensive scheme should include an arrangement under which the youth employment officer, and if necessary the disablement resettlement officer of the Ministry of Labour, joined the team. Emphasizing the importance of the general practitioner, the Minister quoted from the Cohen Report on general practice:

> "The general practitioner, by the exercise of his responsibility for his patient, can link preventive, social and curative medicine. Thus, the general-practitioner service is an essential, not a subordinate service; indeed, in a sense, the general practitioner must hold the key position in the Health Service."

That was true. He believed it to be the true key and link to all co-ordination. He commended the formation and activities of parents' associations. On the problem of spastics in mental deficiency hospitals, the key must be individual treatment. In the follow-up they should watch this of all points most closely, so that not only children in mental deficiency institutions but all spastic children should get the individual attention which in his opinion was the only final answer.

Deaf Children in Mental Institutions

Mr. SOMERVILLE HASTINGS (Barking, Lab.) asked the Minister of Health whether he was aware that a number of children admitted to institutions for the mentally deficient had been proved to be suffering from deafness only; and whether, in view of the improved methods now available for the recognition and treatment of deafness in children, he would give instructions that every child admitted to an institution for the mentally retarded who appeared to be hard of hearing should be examined by an aural specialist on admission and not less than once every five years during

childhood. Mr. IAIN MACLEOD stated on July 1 that he knew of a few such cases, but did not consider that instructions on the lines suggested would be helpful. His officers had recently reviewed the circumstances in which handicapped persons, especially the deaf, might be admitted to mental or mental deficiency hospitals. He understood that there was increasing medical interest in this subject, and that some research was being carried out. He was confident that the medical staff of mental deficiency hospitals made use of improved techniques as they were developed, and arranged for examination by other specialists according to their patients' needs.

45 Copies of Applications

Sir WALDRON SMITHERS (Orpington, C.) asked the Minister of Health on July 1 why it was necessary for applicants for the posts of assistant surgeon (consultant) and part-time anaesthetist (consultant) at Charing Cross Hospital to submit 45 copies of their applications, particulars of which had been sent to him. Mr. IAIN MACLEOD said there was nothing in the regulations governing the appointment of specialists to call for this number of copies of applications, and he was taking the matter up with the board of governors.

Cost of a Drug

Mr. A. BLENKINSOP (Newcastle-upon-Tyne, East, Lab.) asked the Minister of Health whether the preparation "algipan" could be freely prescribed under the National Health Service; and what was its cost, compared with that of any available *B.P.C.* alternative. Miss PAT HORNSBY-SMITH, Parliamentary Secretary, replied on July 1 that a doctor might prescribe any drug or medicine which he considered necessary for the treatment of a patient, but the Joint Committee on Prescribing classified algipan as including drugs which, in their view, had not been proved of therapeutic value. Doctors were therefore asked not to prescribe it unless satisfied it was necessary, exceptionally, in a particular case. The cost to the Health Service was 4s. 6½d. There was no identical standard preparation, but the cost of a similar quantity of a *B.P.C.* ointment commonly used for the same purpose was 2s. 1d.

Cortisone Supplied to Private Patients

Mr. SOMERVILLE HASTINGS (Barking, Lab.) asked the Minister of Health on July 1 whether in cases in which cortisone, A.C.T.H., and other drugs in short supply were prescribed by doctors for their private patients, he would insist that records were kept and made available to his officers. Mr. IAIN MACLEOD stated that records of the amounts supplied to private patients, and the conditions from which they were suffering, were already being made available to his officers.

Ports Medical Service

Mr. H. WATKINSON, Parliamentary Secretary to the Ministry of Labour, stated in answer to Mr. S. AWBERRY (Bristol, Central, Lab.) on June 30 that in 1947 there were 11 medical centres covering three ports, and 128,148 treatments were given, but statistics were not available to distinguish between dock workers and other port workers. By the end of 1953 there were 42 medical centres and seven first-aid rooms established in 30 ports, and during the year treatments were given to 143,826 dock workers and 63,694 others. The National Dock Labour Board hoped to provide medical centres or first-aid rooms in all major ports covered by the national dock labour scheme by the end of this year.

Industrial Diseases.—The Minister of Pensions and National Insurance stated on June 28 that he understood that the Beney Committee appointed to report on industrial diseases not covered by the Industrial Injuries Acts hoped soon to complete the hearing of oral evidence.

Chest Surgery.—The MINISTER OF HEALTH told Mr. SOMERVILLE HASTINGS (Barking, Lab.) on July 1 that at the end of last year major chest surgery was carried out in 73 hospitals under his direction, and there were 81 consultant surgeons engaged on this work.

Medico-Legal

ACTION FOR NEGLIGENCE FAILS

PRINCIPLES RESTATED

[FROM OUR MEDICO-LEGAL CORRESPONDENT]

Lord Justice Denning, sitting as an additional judge of the Queen's Bench Division, in his summing up to the jury in the recent action of *Hatcher v. Black and Others,* restated the principles on which a doctor may be liable in an action for negligence by an aggrieved patient.

The facts were as follows. Mrs. Celia Hatcher, a young married woman of Belgian origin, aged 30, had done free-lance broadcasting work from time to time which required the full use of her voice. She was sent by her doctor to St. Bartholomew's Hospital for examination. There she was seen by Dr. Kenneth Oscar Black, who diagnosed a toxic goitre. He discussed with her the possible alternatives of a partial thyroidectomy or medical treatment, and advised her that operative treatment was the better course. The operation was done by Mr. Edward George Tuckwell, consulting surgeon to the hospital and dean of the medical school. When Mrs. Hatcher asked him on the night before whether there was any risk to her voice, he told her that there was none.

After the operation she found that her voice was not strong. After a fortnight as an in-patient she was sent for three weeks to a convalescent home, and when she returned it was found on examination that her left vocal cord was paralysed. She tried speech therapy with the hospital speech therapist, Miss Joanna Van Thal, who considered that the patient's prospect of recovering a useful voice had been quite good, but that she did not persist. Mrs. Hatcher found that although the quality of her voice was only a little less than before the operation, in use it became weak after a short time, and made her throat painful so that she was no longer able to broadcast.

Mrs. Hatcher's complaint against Dr. Black was that, according to her, he had negligently advised her that operation involved no risk to her voice, and that had she known there was any risk she would have chosen medical treatment, not operation. Her complaint against Mr. Tuckwell was that he had performed the operation negligently, and had damaged her laryngeal nerve. She also complained against both Mr. Tuckwell and the hospital governors that after the operation there had been a negligent failure to discover vocal cord paralysis.

In his summing-up Lord Justice Denning said that Mrs. Hatcher's counsel had compared her case to that of an accident on the road or in a factory. That was the wrong approach, because on the road and in the factory there would be no accidents if everyone used proper care. In hospital, where people who were ill came for treatment, there was always a risk no matter what care was used. It would be wrong, and bad law, to say that simply because a mishap occurred the hospital and the doctors were liable, and it would be disastrous for the community. It would mean that a doctor examining a patient or a surgeon operating at the table instead of getting on with his work would be for ever looking over his shoulder to see if someone was coming up with a dagger. An action for negligence against a doctor was like a dagger which could wound his reputation as severely as it could his body. The jury must not find a doctor negligent simply because one of the risks inherent in an operation had actually taken place, or because in a matter of opinion he had made an error of judgment. A doctor was only negligent when he had fallen short of the standard of reasonable medical care, when he deserved censure. An illustration was the first question raised in the action, what should the doctor tell the patient?

Mr. Tuckwell on the eve of the operation had told Mrs. Hatcher that there was no risk to her voice, although he knew there was some slight risk. This he had done for her own good because of the vital importance to her that

in her condition she should not worry. He had told a lie which in the circumstances was justifiable. It was a matter which in law was left to the conscience of the doctor himself. The law did not condemn him if he did what a wise doctor so placed would do. None of the doctors called as witnesses had suggested that Mr. Tuckwell was wrong to tell her what he had, and if they did not condemn him why should the jury?

Mr. Tuckwell was also charged with carelessness in the operation, and it was said that it was his fault that the nerve was damaged. But all the doctors called as witnesses had said that damage to the recurrent laryngeal nerve was a well-known hazard of the operation even though all care was taken. No doctor called had suggested that Mr. Tuckwell in the course of the operation had done anything he ought not to have done.

As to the complaint about the post-operative period, it was not suggested that the operation injury had been aggravated. The jury might consider whether these complaints had not the colour of ingratitude, and whether Mrs. Hatcher's true nature was not better shown by her letter in which she wrote that she had had nothing but kindness at Barts.

The jury returned a verdict in favour of all the defendants, and judgment was duly entered for them with costs.

The Medical Defence Union instructed Messrs. Hempsons, solicitors, to act for Dr. Black and Mr. Tuckwell.

Vital Statistics

Week Ending June 26

The notifications of infectious diseases in England and Wales during the week included: scarlet fever 770, whooping-cough 2,112, diphtheria 18, measles 2,836, acute pneumonia 286, acute poliomyelitis 53, dysentery 835, paratyphoid fever 16, and typhoid fever 4.

Infectious Diseases

A rise occurred in the number of notifications of infectious diseases in England and Wales during the week ending June 19. The largest increases were 305 for measles, from 2,801 to 3,106, 284 for whooping-cough, from 1,686 to 1,970, and 124 for dysentery, from 772 to 896. The only large fall in incidence was 80 for scarlet fever, from 731 to 651.

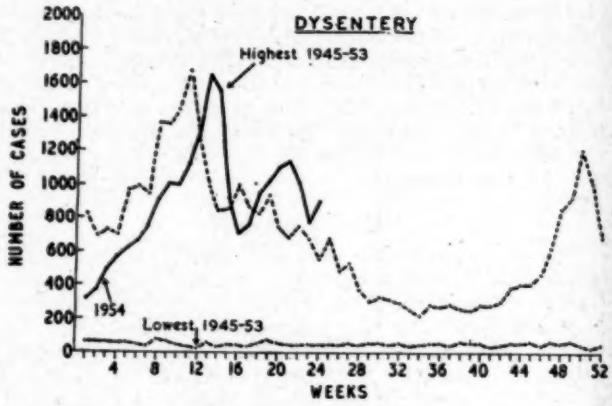
The largest rises in the number of notifications of measles were 150 in Yorkshire North Riding, from 109 to 259 (the rise in this county was due to the outbreak in Middlesbrough C.B., where 215 cases were notified), 74 in Durham, from 212 to 286, 72 in Cheshire, from 189 to 261, and 50 in Norfolk, from 190 to 240, and the largest falls were 96 in Yorkshire West Riding, from 312 to 216, and 59 in Staffordshire, from 167 to 108. The only large increase in the incidence of whooping-cough was 48 in Lancashire, from 173 to 221. 20 cases of diphtheria were notified, being 12 more than in the preceding week. The chief feature of the returns of diphtheria was a rise in Lancashire from 4 to 7 (Liverpool C.B. 6). Only small variations were recorded in the returns for scarlet fever.

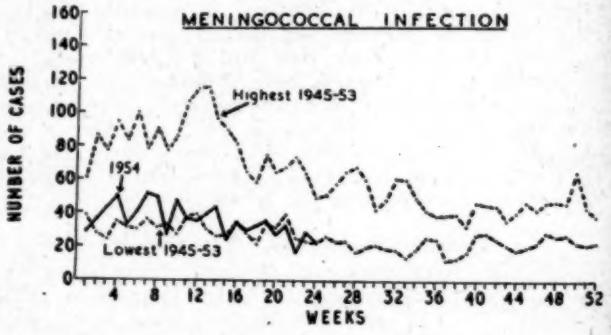
32 cases of acute poliomyelitis were notified. These were 1 fewer for paralytic and 7 more for non-paralytic cases than in the preceding week. The largest returns were Northumberland 6 (Tynemouth C.B. 5), Staffordshire 4 (Walsall C.B. 3), Surrey 3 (Croydon C.B. 2).

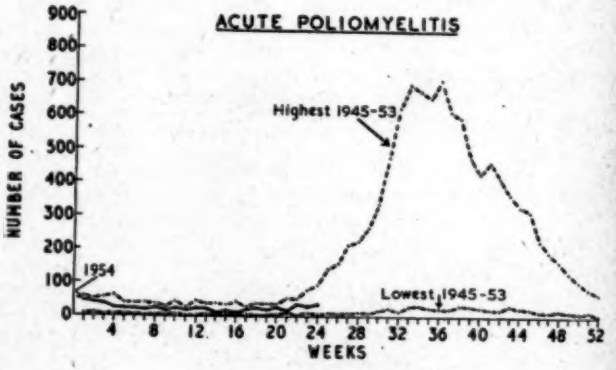
The rise in the incidence of dysentery was mainly contributed by Yorkshire West Riding, with 103 more notifications than in the preceding week. The largest returns were Lancashire 213 (Haydock U.D. 52, Liverpool C.B. 22, Manchester C.B. 16, Irlam U.D. 16, Denton U.D. 10, Prestwick M.B. 19). Yorkshire West Riding 196 (Sheffield C.B. 91, Leeds C.B. 29, Dewsbury C.B. 27, Bradford C.B. 10), London 90 (Islington 20, Lewisham 19), Sussex 57 (Uckfield R.D. 22, Brighton C.B. 20), Leicestershire 46 (Leicester C.B. 40), Cheshire 34, Middlesex 31 (Willesden M.B. 10), Durham 26, and Kent 21.

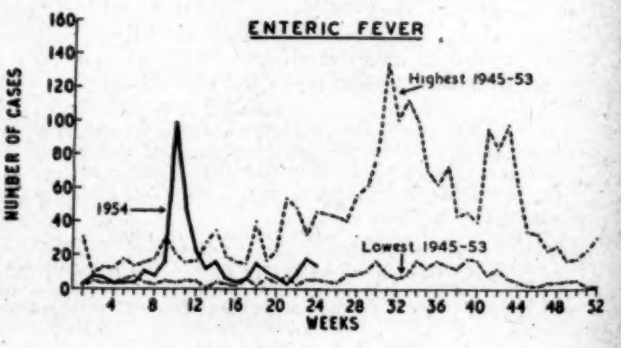
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1945–53 are shown thus -------, the figures for 1954 thus ————. Except for the curves showing notifications in 1954, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **June 19** (No. 24) and corresponding week 1953.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1954					1953				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	20	1	4	0	1	25	1	10	1	
Dysentery	896	90	228	5	4	557	79	171	2	1
Encephalitis, acute	2	0	0	0		9	1	0	0	
Enteric fever:										
Typhoid	3	0	0	1	7	0	0	1	0	
Paratyphoid	11	1	13	0		23	1	2(B)	0	
Food-poisoning	266	22		0		998	16		1	
Infective enteritis or diarrhoea under 2 years				17	19				8	24
Measles*	3,106	93	149	226	345	7,580	291	371	233	210
Meningococcal infection	22	1	19	4	2	27	2	21	1	
Ophthalmia neonatorum	39	1	13	0		37	3	12	1	
Pneumonia†	309	23	124	3	4	370	12	159	6	
Poliomyelitis, acute:										
Paralytic	20	1	13	3		44	3	4	5	2
Non-paralytic	12	1				21	1			
Puerperal fever§	239	35	8	1		261	35	15	2	
Scarlet fever	651	42	107	24	25	1,223	92	193	37	64
Tuberculosis:										
Respiratory	904	121	156	42				164	30	
Non-respiratory	134	12	24	8				40	5	
Whooping-cough	1,970	86	246	29	49	4,104	344	530	61	113

DEATHS in Great Towns	1954					1953				
	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire	Eng. & Wales	Lond.	Scot.	N. Ire.	Eire
Diphtheria	0	0	0	0	0	0	0	0		0
Dysentery	0	0		0		1	1			
Encephalitis, acute		1			0		0			
Enteric fever	0	0	0	0		0	0	0		
Infective enteritis or diarrhoea under 2 years	7	0	1	0	0	6	0	0	0	1
Influenza	2	0	1	1	1	8	0	0	0	0
Measles		0	0	0	1		0	0		0
Meningococcal infection		0	1				0	0		
Pneumonia	154	20	12	5	3	148	20	19	6	4
Poliomyelitis, acute	0	0			0	2	0			1
Scarlet fever		0	0	0	0		0	0		0
Tuberculosis:										
Respiratory	84	12	9	1	4	73	11	7	3	8
Non-respiratory		2	1	0	2		0	3	1	0
Whooping-cough	3	0	0	0	0	4	0	0	0	0
Deaths 0–1 year	222	31	26	5	15	212	17	27	9	14
Deaths (excluding stillbirths)	4,695	666	525	98	149	4,447	596	529	92	127
LIVE BIRTHS	8,436	1197	923	242	419	8,026	1236	937	230	362
STILLBIRTHS	192	19	19			221	29	19		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia.
§ Includes puerperal pyrexia.

Medical News

Honorary Degrees at Glasgow.—During the Annual Meeting of the British Medical Association this week the University of Glasgow conferred the honorary degree of doctor of laws on four medical men: Sir ANDREW DAVIDSON, formerly Chief Medical Officer of the Department of Health for Scotland; Dr. J. B. MILLER, a Vice-President of the B.M.A. and former Chairman of the Representative Body; Mr. J. W. TUDOR THOMAS, immediate Past-President of the B.M.A.; and Sir LIONEL WHITBY, Regius Professor of Physic at Cambridge and President of the B.M.A. in 1948–9. In presenting these four distinguished doctors to the Chancellor of the University, Lord BOYD-ORR, Professor STANLEY ALSTEAD described their achievements in felicitous and telling phrases. Sir Andrew Davidson, he said, was one of that distinguished company of Civil Servants who took pride in the anonymity of their sterling services to the State. "In Dr. Miller," said Professor Alstead, "we recognize a master of the difficult art of general practice. . . . He is a physician who personifies those virtues which have made the Scots doctor a revered figure throughout the world." After referring to Mr. Tudor Thomas's researches on corneal grafting, Professor Alstead spoke of his work as President of the B.M.A. "His ophthalmological training evidently gave him complete insight into the mysteries of this complex organization. . . . [His] presidential tour in the Middle East and further afield succeeded magnificently in its purpose." Presenting Sir Lionel Whitby to the Chancellor, Professor Alstead said that, though his achievements as a research worker, a teacher, and a writer had been acknowledged by the conferment of many honours, Sir Lionel had never lost the common touch. His career epitomized the important contribution that can be made by the practising physician trained in the disciplines of pathology and bacteriology.

Whitley Chair of Biochemistry at Oxford.—Professor H. A. KREBS, F.R.S., who shared last year's Nobel Prize for Medicine and Physiology, has been elected to the Whitley Professorship of Biochemistry at Oxford in succession to Sir RUDOLPH PETERS, F.R.S. Professor Krebs graduated in medicine at Hamburg in 1925. In 1933 with the help of a Rockefeller grant he came to Cambridge as a research student, and two years later he moved to Sheffield under Sir EDWARD MELLANBY, F.R.S. In 1945 he was made professor of biochemistry at Sheffield University, his present appointment. He is also director of the Medical Research Council's cell-metabolism research unit. Professor Krebs is particularly noted for his work on carbohydrate metabolism.

Royal Faculty of Physicians and Surgeons of Glasgow.—On July 5 Sir RUSSELL BRAIN, President of the Royal College of Physicians of London; Sir DAVID CAMPBELL, President of the General Medical Council; Sir JAMES ROGNVALD LEARMONTH, Surgeon to Her Majesty's Medical Household in Scotland and Regius Professor of Clinical Surgery and Professor of Surgery in the University of Edinburgh; and Sir JOHN MCNEE, Emeritus Regius Professor of Practice of Medicine in the University of Glasgow and the new President of the British Medical Association, were admitted to the Honorary Fellowship of the Faculty, having previously been elected Honorary Fellows.

The British Association of Paediatric Surgeons.—The inaugural meeting of the British Association of Paediatric Surgeons last week (see p. 96) concluded with a dinner in the Apothecaries Hall at which the friendly feeling generated during the clinical discussions was fittingly intensified. In a brief speech, Mr. DENIS BROWNE, the president of the new association, said that it had been formed in order to join together those who were interested in the surgery of childhood. He concluded by expressing his gratitude to the eminent surgeons from abroad who had come in such remarkable numbers to the inaugural meeting. Paediatric surgeons from many countries then wished the new associa-

tion well. Dr. G. PETTERSSON (Sweden) said that it was a vigorous baby with excellent possibilities. As a gift from colleagues in Scandinavia he had brought a gavel (handsomely bound in silver) for the president, and he hoped that it would confirm many happy decisions in the history of the association. Dr. ORVAR SWENSON (U.S.A.), Dr. D. VERVAT (Holland), Dr. E. ROVIRALTA (Spain), Dr. C. C. WINKEL SMITH (Denmark), Professor F. REHBEIN (Germany), Dr. M. GROB (Switzerland), Dr. M. SULAMAA (Finland), and Mr. S. T. MCCOLLUM (Eire) all said a few words of greeting. Miss I. FORSHALL (Liverpool) proposed the health of the president and his wife, while Mr. ANDREW LAIRD (Glasgow), Mr. IAN FRASER (Belfast), and Professor NORMAN DOTT (Edinburgh) showed that enthusiasm for the new association was widespread throughout Britain.

British Association of Urological Surgeons.—The tenth annual meeting of the British Association of Urological Surgeons was held in Dublin from June 24 to June 26, under the presidency of Mr. TERENCE MILLIN, and was attended by about 120 members. There was a full scientific programme during the period of the meeting, the main discussion being on "Irradiation Therapy in Urology." The papers will be published in the *British Journal of Urology*. At the annual general meeting the following were elected officers of Council for 1954–5: *President*, Mr. TERENCE MILLIN; *Vice-president*, Mr. R. H. O. B. ROBINSON; *Hon. treasurer*, Mr. J. G. YATES BELL; *Hon. secretary*, Mr. HOWARD G. HANLEY; and *Hon. editorial secretary*, Mr. J. D. FERGUSSON.

The Lister Institute.—In the report of the Governing Body on June 17 to the annual general meeting of the Lister Institute of Preventive Medicine, London, it is stated that the Institute's original endowments no longer suffice to maintain modern developments of research at modern prices. This state of affairs is aggravated by the scientific success of the research work conducted at the Institute. The main divisions at the Institute are: microbiology, immunology, and experimental pathology (under Professor A. A. MILES, director of the Institute); biochemistry (under Professor W. T. J. MORGAN, F.R.S., the deputy director); and biophysics (under Dr. R. A. KEKWICK). In addition there are groups at Elstree concerned with the preparation and study of therapeutic sera, blood products, smallpox vaccine, and bacterial vaccines. At the Institute itself are housed the Medical Research Council's Blood Group Research Unit (director, Dr. R. R. RACE, F.R.S.) and Blood Group Reference Laboratory (director, Dr. A. E. MOURANT).

King Edward's Hospital Fund for London.—The DUKE OF GLOUCESTER presided at the Fund's 57th annual meeting in London on June 30. Reviewing the year's work, he said that direct grants to hospitals, including mental hospitals, and convalescent homes in 1953 had amounted to just on a quarter of a million pounds. The outstanding event of the year had been the establishment of the Matron's Staff College at Holland Park. The Fund had also given evidence before the Guillebaud Committee, which was looking into the cost of the National Health Service, and had recorded its conviction that "as time goes on increasing recognition is likely to be given to the part that voluntary effort and initiative can play in partnership with the State." The treasurer, Sir EDWARD PEACOCK, said that income in 1953 had been £390,000 and expenditure £345,000. The cost of the Staff Colleges and other activities directly administered by the Fund had been £95,000. Sir ERNEST POOLEY, Bt., in moving the adoption of the annual report drew attention to the increased interest the Fund was taking in mental hospitals. Grants totalling about £100,000 had been made to some 20 of these hospitals to help provide better recreational facilities. Sir HAROLD WERNHER, Bt., proposed the vote of thanks to the Duke of Gloucester.

Amphetamine Addiction.—The World Health Organization's expert committee on drugs liable to produce addiction now recommends that amphetamine preparations should be submitted to the same restrictions as barbiturates (*Fourth Report*, March, 1954). In particular the committee suggests that amphetamine and its derivatives should be dispensed only on prescription, and that the prescription should state how many times it may be repeated. A letter on this subject appears in our correspondence columns on p. 101.

1952 in the Factories.—According to the *Annual Report of the Chief Inspector of Factories for the Year 1952* (Cmd. 9154), the numbers of fatal and non-fatal accidents, 792 and 176,718 respectively, were the lowest recorded since the Factories Act, 1937, came into operation. One in every six accidents involved the feet, and a plea is made for a wider use of protective footwear. There were 265 cases of gassing during the year, a higher number than in any year since 1945. Carbon monoxide was responsible in 108 cases, chlorine in 27, and trichlorethylene in 24. There were 217 cases of chrome ulceration and 157 skin cancers. Forty-eight cases of lead poisoning were notified, and 20 cases of anthrax (with one fatality). The use of ionizing radiations in industry has grown steadily, and to meet the situation a pamphlet has been issued on what precautions should be taken to prevent harmful effects (Factory Form 342, price 2s. net, H.M.S.O.).

The Queen's Medical Household.—The Queen has appointed Dr. W. N. MANN, director of the Department of Medicine at Guy's Hospital Medical School, Physician to the Household, and Mr. E. G. MUIR, F.R.C.S., surgeon of King's College Hospital, London, Surgeon to the Household.

Oliver Memorial Fund.—The committee of the Oliver Memorial Fund intend making the seventh award of the value of £50 to a British subject whose original work or services in connexion with blood transfusion is considered to be a notable contribution to the research, organization, or donor aspect of this subject. The committee will welcome applications and, in addition, communications drawing their attention to suitable candidates. Applications must be submitted before August 31 to the honorary treasurer, Mr. F. W. MILLS, c/o National Provincial Bank Ltd., Holborn Circus, London, E.C.1.

Freeze Drying of Microbial Cultures.—During the meeting of the permanent committee of the British Commonwealth Collections of Micro-organisms in London last September, a conference was arranged on the maintenance of cultures by freeze drying. At this meeting technical papers were read and discussed. They have now been collected and published from the British Commonwealth of Nations Scientific Liaison Offices, for the information of interested workers. The pamphlet, entitled "A Discussion on the Maintenance of Cultures by Freeze Drying," is obtainable from Her Majesty's Stationery Office, price 5s. net.

Medical History.—The Wellcome Historical Medical Library has begun publication of a quarterly index to current papers on medical history. Entitled *Current Work in the History of Medicine*, the index will be distributed free to those interested in the subject. It is produced by an offset process. The first number contains references to some 250 papers, arranged in a simple alphabetical sequence of subject headings. This is followed by a personal index of individuals whose life or work forms the subject of a paper, a list of the periodicals indexed (which is only a small proportion of those examined), and those addresses of authors that could be found readily. The index is published by the Wellcome Library at 183, Euston Road, London, N.W.1.

Ciba Foundation.—Professor F. G. YOUNG, F.R.S., professor of biochemistry at Cambridge, and Professor ALEXANDER HADDOW, director of the Chester Beatty Research Institute, Royal Cancer Hospital, London, have joined the executive council of the Ciba Foundation.

R.S.M. President.—Sir WILLIAM GILLIATT has been elected President of the Royal Society of Medicine in succession to Sir FRANCIS WALSHE.

Sir Russell Brain, P.R.C.P., received the honorary degree of D.C.L. of Durham University on July 3.

COMING EVENTS

John Tate Memorial Lecture.—Sir HENRY COHEN will speak on "The Role of the Laboratory in Clinical Medicine" on July 21 at 5.30 p.m., at the Middlesex Guildhall, Westminster, S.W.1.

Health Education.—The Central Council for Health Education will hold a summer school on August 17–27 at Bangor, North Wales, on the subject "Programme and Practice in Health Education." Lecturers will include Professor F. A. E. CREW, F.R.S., and Dr. GRANTLY DICK READ. Details from the Medical Director, Central Council for Health Education, Tavistock House, Tavistock Square, London, W.C.1.

SOCIETIES AND LECTURES

A fee is charged or a ticket is required for attending lectures marked ●. Application should be made first to the institution concerned.

Monday, July 12

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Joseph Henry Lecture by Dr. R. A. M. Case: Tumours of the Urinary Bladder as an Occupational Disease.

Tuesday, July 13

●INSTITUTE OF NEUROLOGY.—5.30 p.m., Dr. J. St. C. Elkington: Cerebral Infarction.

Wednesday, July 14

OXFORD UNIVERSITY.—At Radcliffe Infirmary, 5 p.m., Dr. Morris C. Davis (University of Melbourne): Use of Special Visual-aid Techniques in the Integrated Teaching of Clinical Medicine.

Thursday, July 15

●INSTITUTE OF NEUROLOGY.—5.30 p.m., Dr. David Sutton: Radiology of Traumatic States.

ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE.—At Hospital for Tropical Diseases, 4, St. Pancras Way, London, N.W.1, 7.30 p.m., clinical meeting. Cases and pathological specimens will be demonstrated.

Friday, July 16

BIOCHEMICAL SOCIETY.—At Department of Biochemistry, Queen's University, Belfast, 11 a.m., 331st meeting. Scientific papers will be read.

ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Charles Tomes Lecture by Professor M. A. Rushton: Anomalies of Human Dentine.

APPOINTMENTS

NORTH-EAST METROPOLITAN REGIONAL HOSPITAL BOARD.—Helen M. Mayer, M.R.C.S., L.R.C.P., M.R.C.O.G., Part-time Consultant Obstetrician and Gynaecologist, Forest Gate Hospital; I. L. M. Larkin, M.D., Full-time Consultant Pathologist, Oldchurch and other hospitals in the Romford Group; F. McL. McGown, M.D., M.R.C.P., Full or Maximum Part-time Consultant Physician, Oldchurch and St. George's, Hornchurch, Hospitals; Frances Gardner, M.D., F.R.C.P., Part-time Consultant Physician, The Mother's (Salvation Army) and Thorpe Coombe Maternity Hospitals; P. J. Carter, F.R.C.S., D.L.O., Part-time Consultant Ear, Nose and Throat Surgeon, Tilbury and Riverside Hospitals; Vivien U. Lutwyche, M.D., M.R.C.P., Full-time Consultant Chest Physician, Epping and Buckhurst Hill Chest Clinics; E. M. C. Dunlop, M.D., M.R.C.P., Part-time Consultant Venereologist, Metropolitan Hospital; A. J. Freese, F.R.C.S.Ed., L.D.S., Part-time Consultant Dental Surgeon, Victoria Hospital, Romford; J. N. Milnes, M.D., M.R.C.P., Part-time Consultant Neurologist, Metropolitan Hospital; Marcia I. P. Wilkinson, B.M., B.Ch., M.R.C.P., Part-time Consultant Neurologist, St. Margaret's Hospital, Epping; T. E. Broadbent, M.B., Ch.B., D.M.R.D., Full- or Maximum Part-time Consultant Radiologist, North Middlesex Hospital and Annexes.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Edelman.—On July 2, 1954, at Hillingdon Hospital, Middlesex, to Jacqueline (formerly Heller), wife of Dr. Seymour Edelman, of 267, Church Road, Hayes, Middlesex, a brother for Ian—Roger Adrian.

Elliott-Binns.—On June 26, 1954, at the Barrett Maternity Home, Northampton, to Cicely, wife of Dr. C. P. Elliott-Binns, a daughter—Jane Elizabeth.

Ring.—On June 30, 1954, in London, to Stella, wife of Mr. Peter Ring, F.R.C.S., a son.

Tepper.—On July 4, 1954, at Brighton General Hospital, to Drs. Rachel (formerly Claiman) and Raphael Tepper, a brother for Jane.

DEATHS

Davidson.—On June 12, 1954, at R.N. Hospital, Great Yarmouth, Norfolk, Arthur Robertson Davidson, M.B., Ch.B., Surgeon Captain, R.N., retired.

Davies.—On June 14, 1954, Josephine Margaret Davies (formerly Howells), M.R.C.S., L.R.C.P., D.P.H., of Bryn-y-Wawr, Llandilo, Carmarthenshire, late of Caerphilly, near Cardiff.

Hickley.—On June 15, 1954, at his home, "Lonmay," Beaconsfield, Bucks, Thomas Brooke Hickley, M.R.C.S., L.R.C.P.

Johnstone.—On June 14, 1954, at "Highroyds," Menston, near Leeds, Yorks, John Stephen Johnstone, M.B., Ch.B., Dipl. Psych., formerly of Aberdeen, aged 45.

MacGregor.—On June 6, 1954, at 71, Fuller's Road, Chatswood, New South Wales, Australia, James MacGregor, *M.C.*, M.D., Group Captain, R.A.F., M.S., retired.

McKee.—On June 16, 1954, at 9, Molesworth Terrace, Stoke, Plymouth, Devon, Thomas Barrington McKee, *M.C.*, M.D., D.P.H.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

First-aid Dressings for Burns

Q.—*What is the best dressing to apply to burns of exposed skin? Official first-aid handbooks mention both dry dressings and dressings soaked in a bicarbonate solution. The underlying principle seems to be agreed that what is wanted is to exclude air and relieve pain. I think there can be no doubt that cold wet dressings on the actual burn relieve the pain far better than a dry one. What would your expert advise?*

A.—The pain and hyperalgesia following superficial burns are relieved by cooling applications and by protecting the surface from external stimuli. On these grounds, dressings soaked in bicarbonate solution are likely to be superior to dry dressings for relieving pain and discomfort. On the other hand, the painful condition usually lasts only a few minutes, and a far more important consideration for the healing of the burn is whether it should become septic. Any wet dressing is more liable to permit infection to pass through from the outside, and furthermore it is difficult to ensure that, unless freshly prepared with sterile materials, the bicarbonate solution is itself free from organisms. An application which meets both criticisms is a cream such as penicillin cream *B.P.*, which is both cooling and active in preventing the more severe types of infection. For the large burn, time which would be spent in devising and applying local dressings is much better employed in ensuring rapid transport to hospital. For such cases a freshly laundered or sterile cloth to cover the area is the local first-aid treatment of choice.

Rescue and Treatment after Electrocution

Q.—*A person has been rendered unconscious by contact with a high-voltage cable. In such an emergency: (1) What is the safest way of removing him from contact with the source of electricity, it being assumed that articles such as rubber gloves are not immediately available? (2) How should he be treated, and for how long should artificial respiration be performed before it is abandoned? (3) Are there any risks of the victim remaining charged after breaking the contact, and, if so, what precautions should the rescuers take? (4) What is the prognosis, and what factors influence it?*

A.—(1) There is no safe way for the uninitiated to remove a person from contact with a high-voltage cable. It cannot be stressed too strongly that such a procedure is extremely likely to produce two victims instead of one. The following comments, however, might be of interest.

Presumably the words "high voltage" mean something of the order of 6.6 kV upwards—that is, up to 275 kV, the voltage of the supergrid—and the only way a person could come into contact with voltages of this type would be by overhead cables or by climbing into a substation and coming into contact with some of the live conductors on the equipment. At 6.6 kV and above, persons rarely continue in contact, for the simple reason that the current jumps across from the conductor to the person's body before contact is made. This generally has the effect of throwing him off, and in many cases considerable arcing occurs which involves the person in extensive burns. This arcing may be the means of automatically disconnecting the circuit, but there would be no definite indication of this to a would-be rescuer. If the victim of a shock is unfortunate enough to fall across a live high-voltage conductor and remain in

contact, the chances of him surviving are so small as to make it foolish to try to pull him off. If, however, he has fallen clear, and any person wishes to risk his life in getting the victim into such a position as to enable first-aid attention to be given, then I should say that the best means of removing him would be with a long, dry pole or a long, dry rope, used in such a way as to keep the rescuer completely clear of the electrical equipment. Even this may be dangerous advice, because the pole or rope which would be suitable for 6.6 kV would be totally unsuitable in length for 132 or 275 kV. It is on account of such considerations that I think that any attempt at all at rescue by a person with insufficient knowledge of the electrical system concerned would be accompanied by very grave danger.

In the case of contact with a live electric rail, there are certain important differences. In Britain the railways use a *direct* current at a voltage of 600—much lower than that envisaged above. Further, the current is automatically switched off if there is a short circuit. It is, in spite of newspaper reports, rather unusual for contact with a live rail to cause death. Lastly, a direct current has not the nasty trick that an alternating current has of making it impossible to let go.

(2) The treatment is the normal treatment for shock. Artificial respiration is required only when breathing is imperceptible. It should be carried on for at least two hours. It is sometimes urged that it should be continued until cooling of the body or rigor mortis indicates death.

(3) There is no danger of the victim remaining charged after breaking contact, for the simple reason that if he is receiving an electric shock some part of him must be in contact with earth. It is conceivable but highly improbable that he would be resting on two live conductors without touching earth, but immediately on falling from these conductors he would make sufficient contact with earth to make the possibility of anybody receiving a static shock from his body negligible.

(4) It is advisable in all cases of electric shock where consciousness has been lost to keep the patient recumbent for 24 hours. Particular care should be taken to examine the cardiac function. If the patient recovers consciousness the prognosis is good and no particular factors will influence it. It must be remembered, however, that severe cases of electric shock are accompanied by burns.

Aluminium for Cooking

Q.—*Are there any dangers from using aluminium utensils for cooking? Are some people unduly sensitive to aluminium?*

A.—There are no dangers from using aluminium utensils for cooking. This question has been investigated very thoroughly, and the results have established that of all the metals aluminium is the least toxic. It is less toxic than iron, and no cases of persons being sensitive to aluminium have been established. A report on this question was published by the British Non-Ferrous Metals Research Association (External Series, No. 162) in 1932.

Treatment of Flushing

Q.—*What are the causes and treatment of flushing, as distinct from blushing? The patient, a man of 21, is of good physique and has no other symptoms. The attacks of flushing of the face come on at any time, during a meal, at the pictures, when going for a walk, etc. The patient finds the condition most uncomfortable and sometimes embarrassing.*

A.—Flushing is due to vasomotor instability and may occur in hyperthyroidism, hypogonadism, or without any obvious cause. The case in question appears to belong to the last category and treatment is likely to prove unsatisfactory. Overloading the stomach and alcohol should be avoided, and small doses of a sedative—e.g., phenobarbitone, ¼ to ½ gr. (16 to 32 mg.) three times daily—together with a vasoconstricting drug such as ephedrine, ½ to 1 gr. (32 to 65 mg.) three times daily, may be tried.

Inheritance of Deaf-mutism

Q.—*A healthy young man wishes to marry a healthy girl of about the same age. She has six sisters, all healthy, but three brothers, all mute and deaf. What are the chances of these defects appearing in this couple's offspring? They cannot trace any similar defects in their other relatives.*

A.—From the particulars given it must be assumed that the three brothers of the girl suffer from genetic deaf-mutism. This is due to a recessive gene, so there are two chances in three that she is a carrier. As the man has no history of deaf-mutism in his family, and assuming that he and the girl are not blood-relatives, the chance that he too is a carrier is remote. The risk that any of their children will be deaf-mutes is smaller than the risk that some serious congenital defect or other will occur in any random pregnancy. Thus the extra risk that this couple would be running may fairly be dismissed as negligible. It is far smaller than that taken whenever a Rhesus-negative woman marries a Rhesus-positive man, which happens in one marriage in every eight in this country. Nor need the girl feel any doubts about the possibility of passing on the gene to her children; in all probability we all carry at least one seriously harmful recessive gene, so if it was not this one it would be some other kind instead.

Treatment of Cysticercosis

Q.—*Is there any useful treatment for cysticercosis, apart from dealing with symptoms as they come?*

A.—No, there is none of any proved value. Fortunately, the prognosis of cysticercosis is often favourable, even in cases in which epilepsy arises. Adequate symptomatic treatment and control of fits are therefore well worth while, and if continued for a period, which may need to be of several years' duration, the fits commonly become less frequent and cease permanently.

NOTES AND COMMENTS

Oestrogen in Mumps.—Dr. G. G. JENNER (Dunedin, New Zealand) writes: Your correspondent inquires about the use of hormones in mumps oophoritis ("Any Questions?" April 10, p. 888). R. Crosnier[1] makes the following statement: "In case of mastitis, ovarian pain, or oophoritis in the woman or pubescent girl, rare incidents (rather than complications), use could be made of testosterone." He goes on to cast doubt as to whether sterility following such oophoritis is entirely due to the mumps.

REFERENCE

[1] *Presse Médicale*, 1952, **60**, 1398.

Corrections

On p. 1506 of the July 26 issue of the *Journal*, "National Federation for Polio Research" should have read "National Fund for Polio Research."

We regret that among the signatures to the letter on "Medical Hypnosis" (July 3, p. 51) the name of Dr. W. Moodie was misspelt.

Refresher Course Books.—The first two volumes of collected articles from the Refresher Course for General Practitioners published in the *Journal* are now available. The first volume contains 55 articles and the second 60. Each article has been revised by its author. Copies of both volumes may be obtained, price 25s. (postage 1s.) each, direct from the Publishing Manager, B.M.A. House, Tavistock Square, London, W.C.1, or from booksellers. The second book of **"Any Questions?"** is also available, price 7s. 6d. (postage 6d.).

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